SIMULATION STUDY TO EXPLORE THE HEALTH EQUITY IMPACT OF A HYPOTHETICAL NEW CANCER THERAPY AS A FUNCTION OF TREATMENT AND DISEASE CHARACTERISTICS

MSR2

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BACKGROUND

- In the context of a sharper focus on health equity, the question that comes to mind as part of the discussion about the value of a new intervention is whether it is likely to reduce or increase disparities in health outcomes.[1-5]
- A new intervention that is effective will attenuate or exacerbate inequality in health outcomes in the target patient population of interest, if there is heterogeneity between equity relevant subgroups in:
  - (i) baseline event or outcome probabilities;
  - (ii) relative treatment effects; or
  - (iii) uptake.[6]
- Opportunity costs need to be considered as well.
- Cancer is characterized by ongoing disparities in incidence rates, treatment, and outcomes.[7,8] More than 1300 compounds are currently in development as cancer therapy.[9]
- Understanding when a new cancer therapy can have a meaningful impact on inequality in outcomes is valuable information for HTA decision-makers and to inform drug development decisions.

OBJECTIVE

To perform a simulation to investigate the health equity impact (HEI) of a hypothetical new cancer therapy as a function of treatment and disease characteristics using the distributional cost-effectiveness analysis (DCEA) framework.[10-12]

METHODS

- The following scenario was represented: A comparison of a new therapy versus standard of care (SOC) for the treatment of a specific cancer patient population that consists of four subgroups according to race/ethnicity with the aim of preventing disease progression and improving survival.
- Simulations were performed with a 3-state partitioned survival model (PSM) based on progression free survival (PFS) and overall survival (OS) curves that varied by treatment and subgroup of the target patient population.[13,14]
- The expected net health benefit (NHB = quality adjusted life-years [QALYs] – costs/opportunity cost threshold) was calculated for both treatments by subgroup assuming equally distributed opportunity costs.
- The HEI from a change in inequality in the NHBs across subgroups with the new therapy relative to SOC was expressed with Atkinson and Kolm inequality metrics.[15,17]
- **Figure 1** provides an overview of the concept of this study.
- Importance of factors related to outcomes under both treatments, health state utility and cost values, the opportunity cost threshold, and degree of inequality aversion for the estimated health equity impact of the new intervention were evaluated in 5000 simulations. (See **Table 1**)
- The simulation study was “tumor type and treatment line agnostic" with parameter values informed by multiple cancer conditions.
- All simulations were performed with R statistical software using the hesim package.[18]

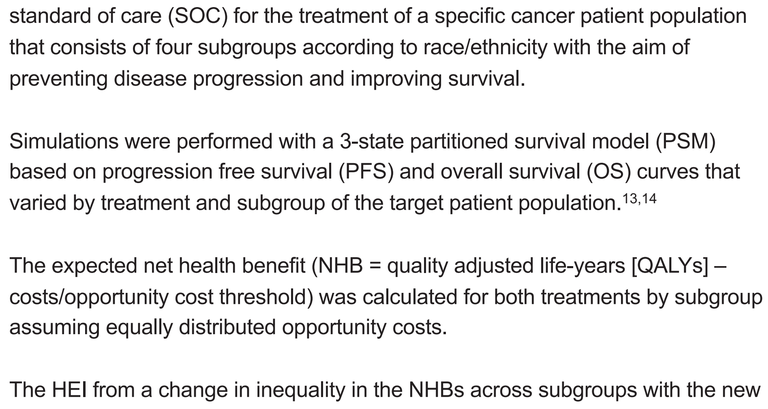

Figure 1: Parameters that were varied in the simulation of the health equity impact of a new cancer therapy

Table 1: Parameter values used in the simulation

	Input parameter	Low	High
PFS and OS curves with SOC for subgroup 1	Shape (of Weibull distribution) PFS and OS	1	2
	Scale (of Weibull distribution) OS	0.6	1
	Multiplier OS scale to obtain PFS scale	1.1	1.5
Prognostic effect of sub-population characteristics	Hazard ratio from one subgroup to the next	0.67	1.5
Relative treatment effect of New vs. SOC	Hazard ratio	0.5	1
Effect modification of subgroup characteristics	Ratio of hazard ratio New vs. SOC from one subgroup to the next	0.67	1.5
Utility	Pre-progression	0.7	1
	Post-progression	0.4	0.7
Drug cost (per year)	SOC	500	500
	New	500	20,000
Other medical cost	Pre-progression	1,000	5,000
	Post-progression	2,000	15,000
Other	Opportunity cost threshold	100,000 In sensitivity analyses set at 50,000 and 150,000	
	Atkinson inequality aversion parameter	11 In sensitivity analyses set at 2 and 19	
	Kolm inequality aversion parameter	0.15 In sensitivity analyses set at 0.005 and 0.30	

RESULTS

- The most important factors impacting HEI on a relative and absolute scale were
  - the extent of between-subgroup heterogeneity in relative treatment effects (i.e., the degree of effect-modification);
  - differences in PFS and OS between subgroups with SOC (i.e., the prognostic effect);
  - the shape of the PFS and OS curves; and
  - the difference in drug costs between the new therapy and SOC.
- **Figure 2** shows the Atkinson-based HEI as a function of the degree of prognostic effect and effect-modification.
  - The relative inequality in health outcomes *increased* (i.e., negative HEI) when the relative treatment effects with the new therapy were the worst for the subgroups with the worst PFS and OS under SOC.
  - Similarly, the relative inequality in health outcomes *decreased* (i.e., positive HEI) when the relative treatment effects with the new intervention were the best for the subgroups with the worst PFS and OS under SOC.
  - The largest effect on relative HEI metrics was observed when the SOC PFS and OS hazard rates and the new therapy hazard ratios differed at least 10% between two subgroups.

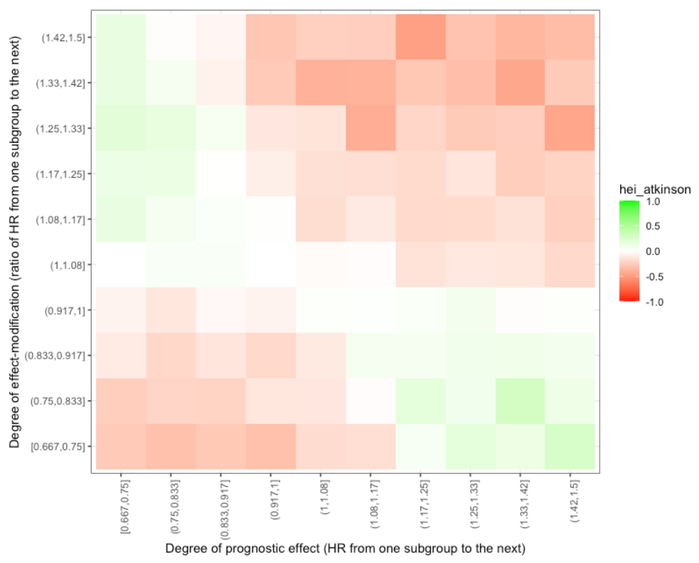

Figure 2: Health equity impact (Atkinson) of a new therapy as a function of the degree of prognostic effect and effect-modification between subgroups

- The impact of the combination of the degree of prognostic effect and effect-modification on relative inequality in health outcomes increased when PFS and OS with SOC was larger (**Figure 3**), and when the new therapy was more expensive (**Figure 4**).

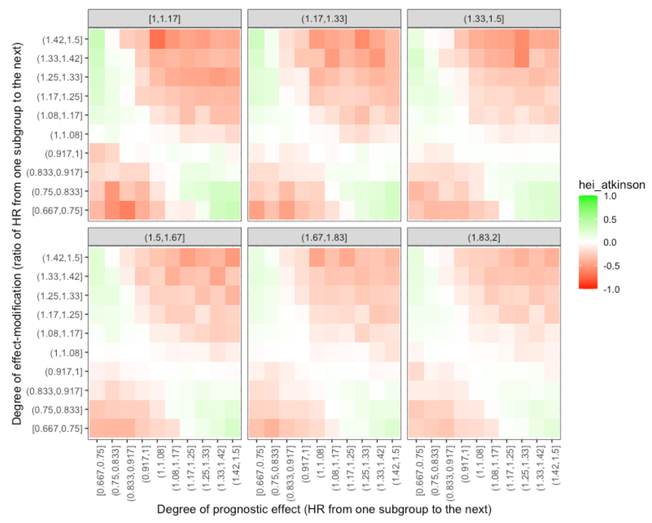

Figure 3: Health equity impact (Atkinson) as a function of the degree of prognostic effect and effect-modification by shape of the survival curves under SOC. Each of the 6 panels from left to right represents increased values for the shape parameters of the PFS and OS curves with standard of care corresponding to a shorter expected PFS and OS

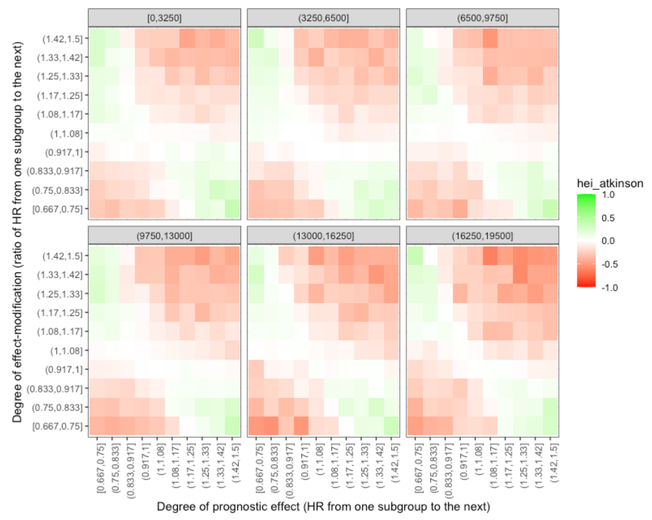

Figure 4: Health equity impact (Atkinson) as a function of the degree of prognostic effect and effect-modification by increase in drug cost with the new therapy. Each panel from left to right shows increasingly greater drug costs

- Larger inequality aversion and lower opportunity cost thresholds magnified the positive or negative HEI of the new therapy and the impact of the above-mentioned factors.
- The patterns observed regarding Atkinson-based HEI in relation to the impactful factors were also observed for the Kolm-based HEI evaluations, but with the impact of the different factors less pronounced.

DISCUSSION

- With the simulations we made the following simplifying assumptions to facilitate interpretation:
- A change in the distribution of health outcomes across subgroups with the new therapy versus SOC was defined as HEI.
- The subgroups of interest for the HEI were homogenous groups where each individual experiences the same prognostic effect and relative treatment effect.
- Differences in the prognostic effect or relative treatment effect from one subgroup to the next were assumed to be constant on a ratio scale with the smallest impact in subgroup 1 and the largest impact in subgroup 4.
- The prognostic effect and effect-modifier only impacted the scale parameter of the PFS and OS curves thereby defining that the PFS and OS curves by subgroup run parallel and do not cross.
- Equally shared health opportunity costs across the subgroups.
- Differential uptake of the new therapy across subgroups was not incorporated.

CONCLUSION

- A new cancer treatment’s impact on inequality in health outcomes was reduced (increased) when its efficacy was better (worse) among the sub-populations benefitting the least from SOC.
- The largest effect on health equity impact metrics was observed when the relative treatment effects with the new intervention and PFS/OS hazard rates with SOC varied at least 10% between two subgroups.
- The impact of these two factors was amplified when a cancer had longer PFS and OS, the difference in treatment costs increased, inequality aversion was larger, or the opportunity cost threshold was lower.

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