Tailoring decision making to reflect patient preferences and expected treatment outcomes

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Paradigm shift toward patient-centered care

- Incorporating a patient's preferences for care
- "Preference-sensitive" decision = choosing among several medically appropriate treatments

However, in practice

- Clinicians still dominates many cancer treatment choices [1]
- Physicians may recommend more aggressive treatments for patients than they would prefer for themselves [2]
- Physicians may not accurately perceive patient preferences [3]

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[1] Gaston and Mitchell 2005 *Social Science and Medicine*
[2] Ubel et al. 2011 *Archives of Internal Medicine*
[3] Elkin et al. 2007 *Journal of Clinical Oncology*

Medical decision making is complex

Shared decision making requires relevant, personalized information to inform treatment choices.

- Limited number of tools exist to assist clinicians and patients
- Our focus is defining a statistical approach to rank treatments based on both predicted treatment effectiveness and patient preferences

Measuring health preferences with utilities

- Health utilities = self-reported evaluations of health states
- Measured on 0 (death) - 1 scale (perfect health)
  - 0.85 utility = health state with 15% less quality of life than perfect health
- Health utilities typically examined on a population level

Previous studies provide evidence of preference heterogeneity

Prostate cancer patients [4]

1. Strongly valued survival time, willing to tolerate side effects
2. Willing to trade survival time for diminished side effects
3. Preferred status quo / watchful waiting

[4] Meghani et al. 2009 *BMC Medical Informatics and Decision Making*

Objectives of our study

1. Examine preference heterogeneity in colorectal cancer setting
2. Estimate expected outcomes under 3 chemotherapy regimens using hierarchical Bayesian model
3. Define preference-weighted outcome score (PWOS) to rank treatments based on both predicted outcomes and preferences
4. Apply preference-weighted outcome score to RCT data and simulated data

I. Examining heterogeneity in colorectal cancer

Utilities assessed for 4 health states [5]

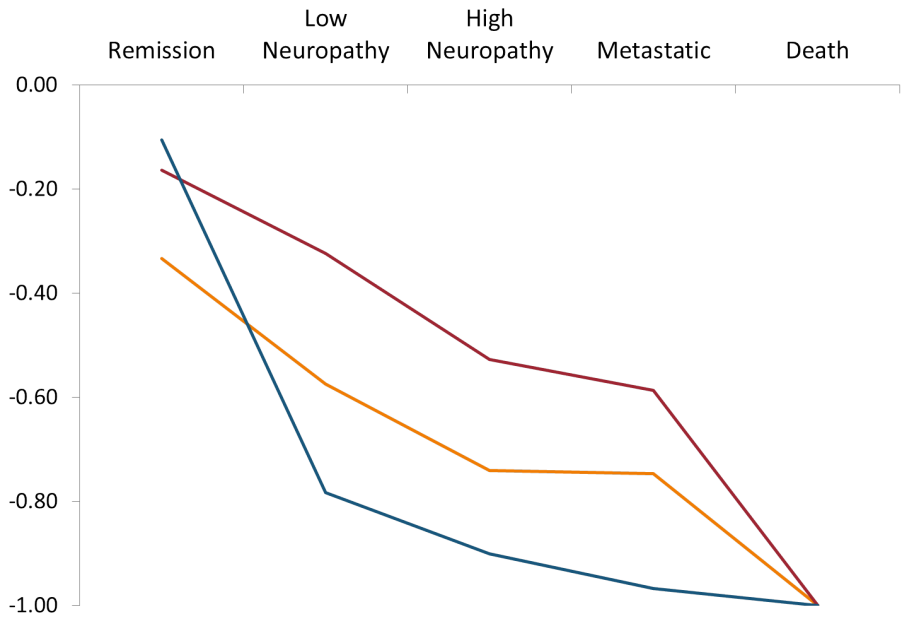
- Remission
- Adjuvant chemotherapy with no / mild neuropathy
- Adjuvant chemotherapy with moderate / severe neuropathy
- Metastatic disease

n =49 colorectal cancer patients + 49 community members

[5] Best et al. 2010 *Quality of Life Research*

Latent profile analysis: observed heterogeneity

	Disutility values		
	Class 1	Class 2	Class 3
	(n=51)	(n=42)	(n=5)
Remission	-0.16	-0.33	-0.11
Low Neuropathy	-0.32	-0.57	-0.78
High Neuropathy	-0.53	-0.74	-0.90
Metastatic disease	-0.59	-0.75	-0.97



II. Using RCT data to model multiple colorectal outcomes

7 historical trials of 3 adjuvant chemotherapy regimens

Treatment	Study arms	Combined *n*
FULV	7	4446
FOLFLOX	2	2332
XELOX	1	938

5 yr outcome	(Ref)		
Living w recurrent disease	<1 yr	1-2 yrs	2+ yrs
(Early) Death	<1 yrs	1+ yrs	
Diarrhea	none	any	
Leuko/neutropenia	none	mild/moderate	severe
Nausea/vomiting	none	mild/moderate	severe

Note: no overlap between trial outcomes and health utility measures

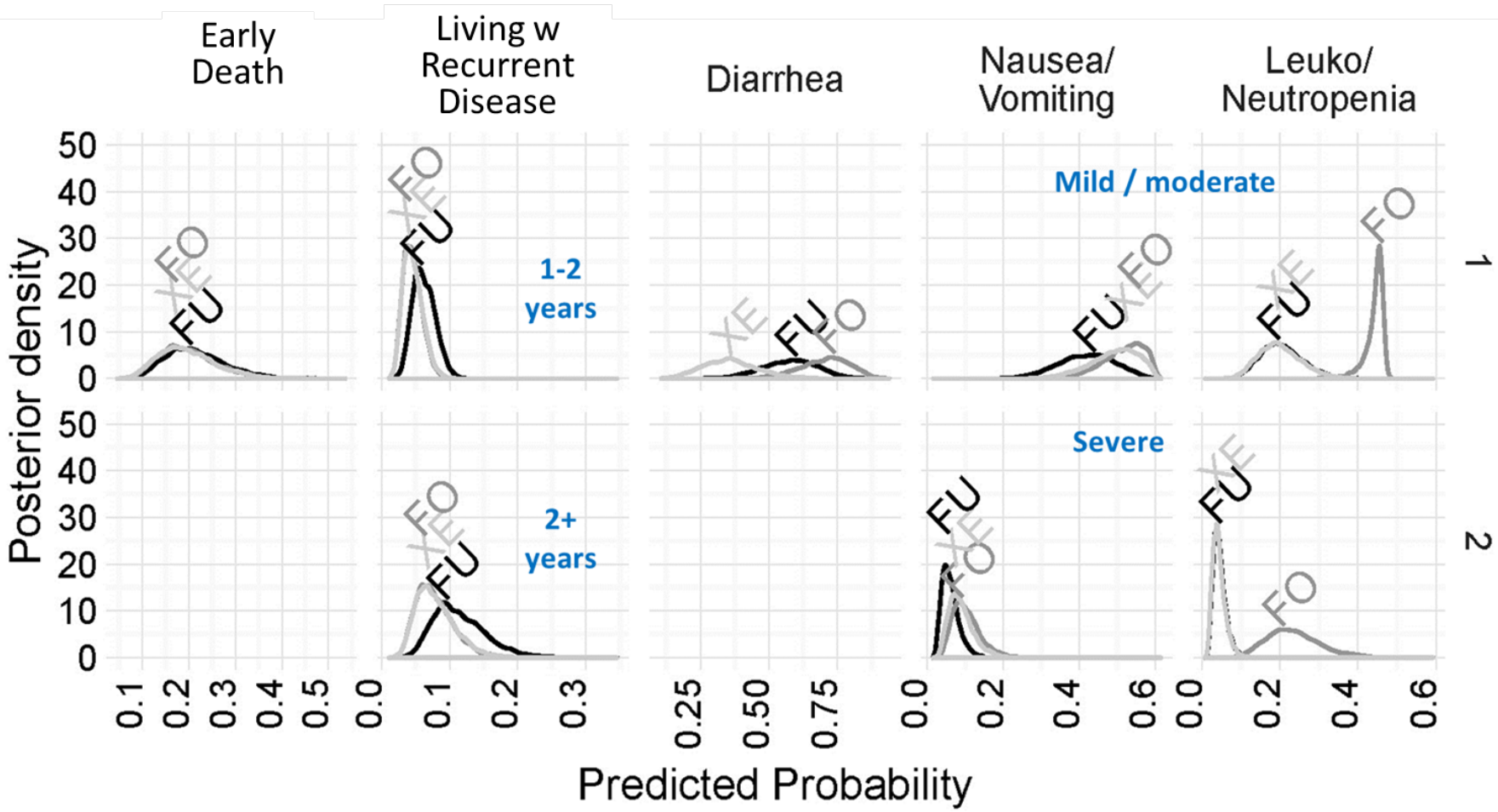
Bayesian joint outcome model

- Outcome k at level ℓ of person i in study j:

$$Pr(y_{ijk} = \ell) = f(\beta_{0jk} + \beta_{1k} trt_{ij} + \gamma_k u_{ij}, \tau_k)$$
$$\beta_{0j} \sim N(\beta_0, \Sigma)$$
$$u_{ij} \sim N(0, \sigma_u^2)$$

- Joint model accounts for correlation across outcomes
- Fit ordinal probit model using rjags; prediction model omits person-level random effects

Predicted probabilities of 5 outcomes



FU = FULV, FO = FOLFOX, XE = XELOX

III. Preference-weighted outcome score (PWOS)

Sum of predicted outcomes, weighted by health utilities

$$\psi(u_i, y^{trt}) = \sum_k \sum_{\ell \in \mathcal{L}_k} u_{ik\ell} P(y_k = \ell | trt)$$

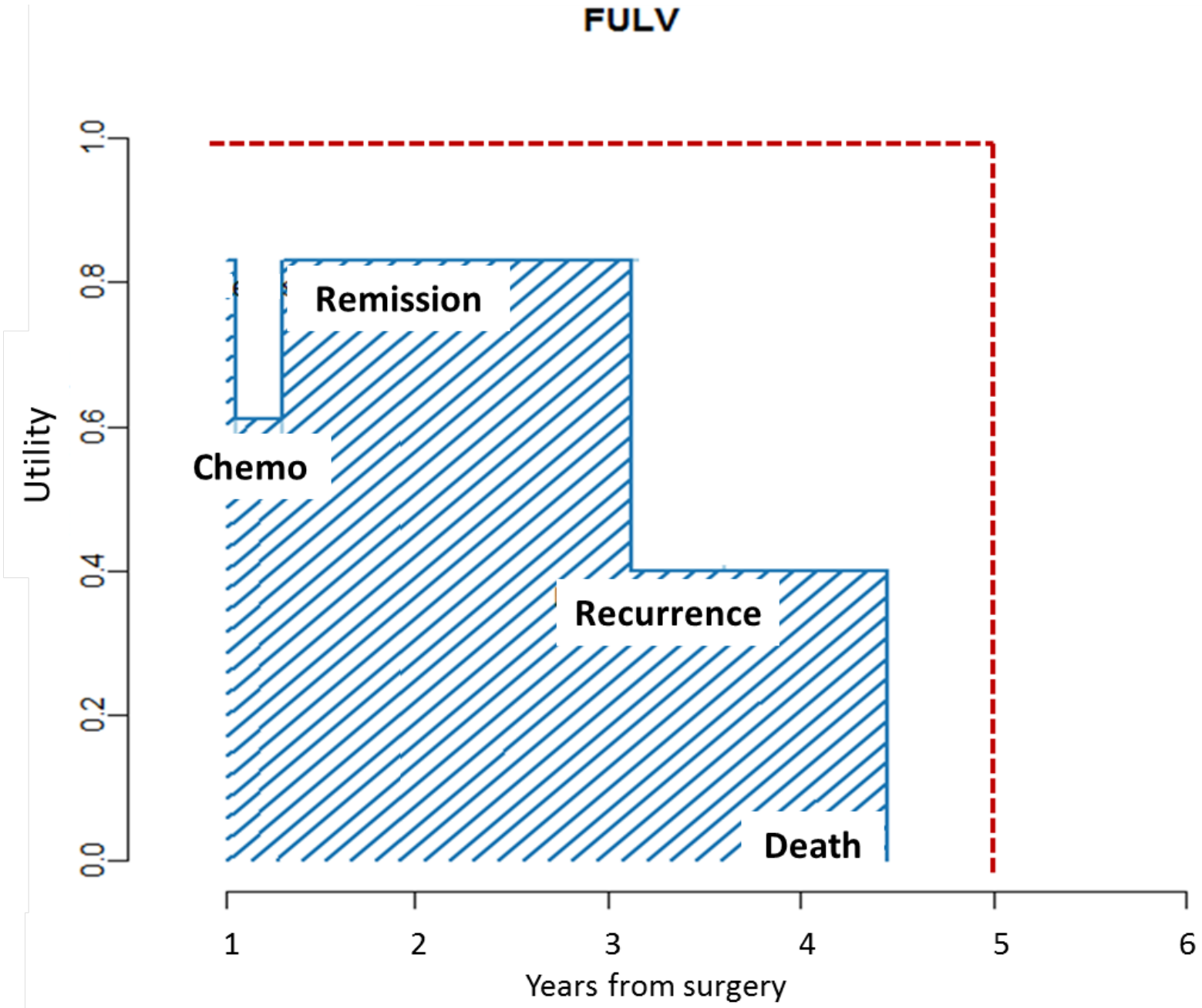
$u_{ik\ell}$ scaled as disutilities

Time-weighted version

$$\psi(u_i, y^{trt}, w) = \sum_k \sum_{\ell \in \mathcal{L}_k} w_{k\ell} u_{ik\ell} P(y_k = \ell | trt)$$

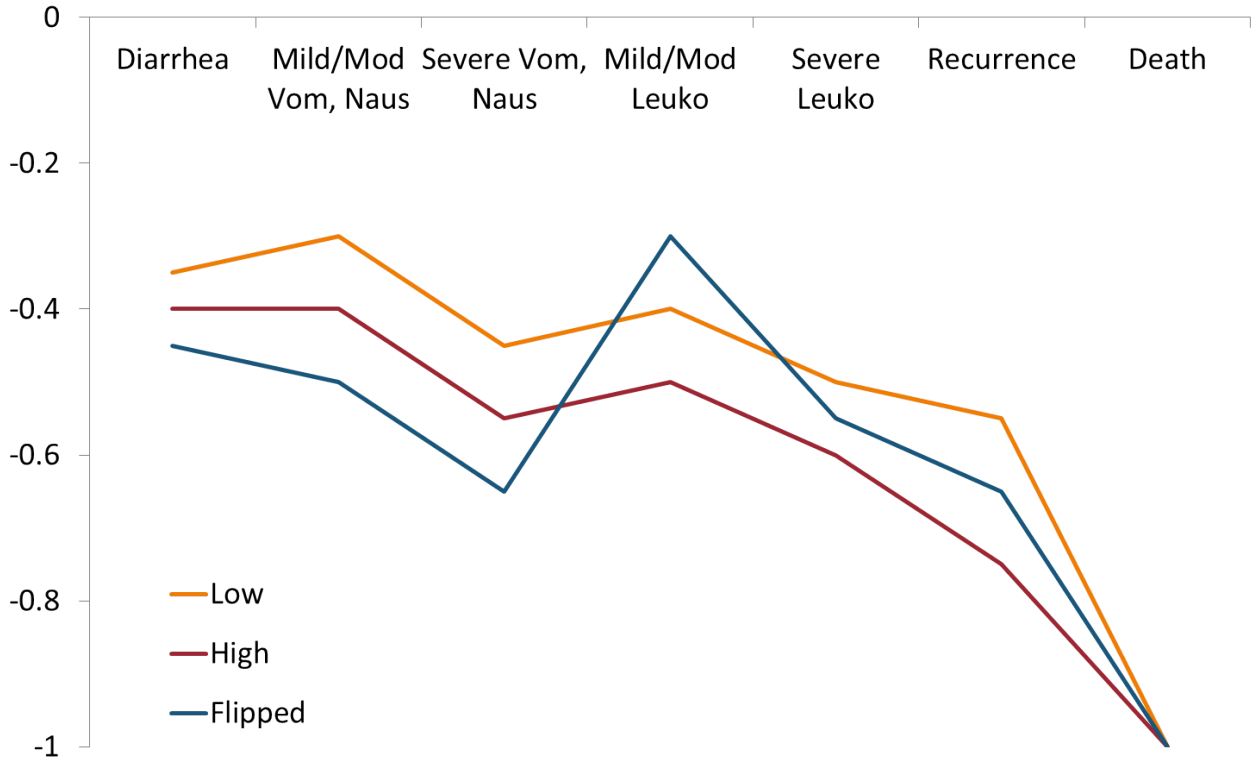
$w_{k\ell}$ scaled as proportion of follow-up time

Preference-weighted outcome score (PWOS)



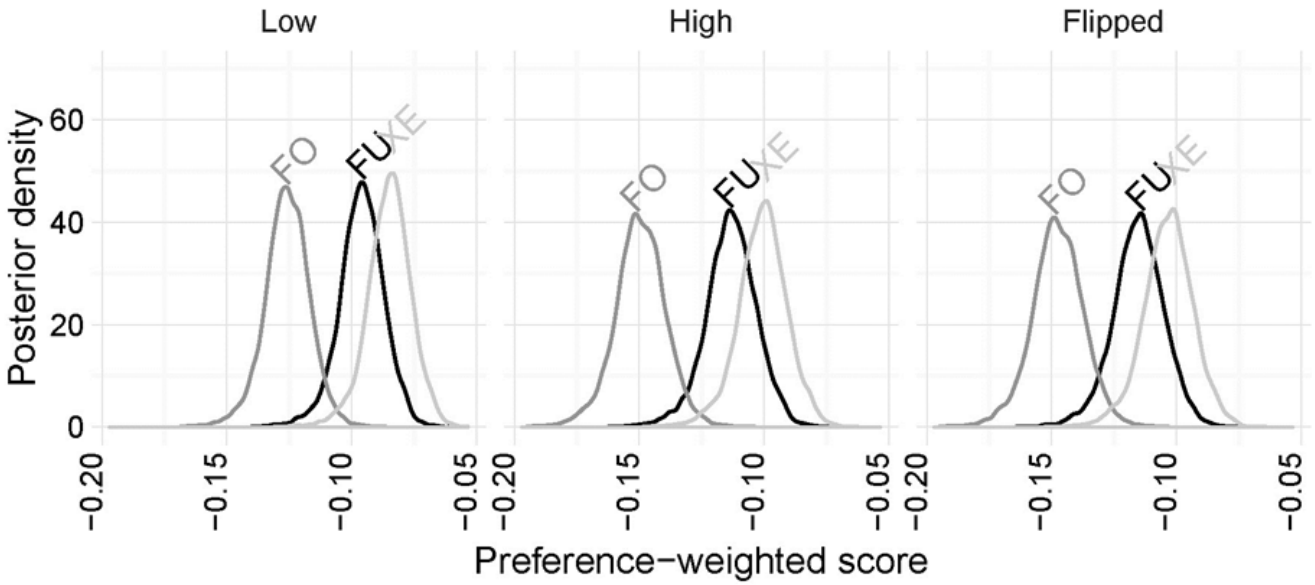
Generated illustrative preference profiles

- RCTs did not collect utilities data
  1. **Low sensitivity:** Adverse events less burdensome
  2. **High sensitivity:** Adverse events more burdensome
  3. **Flipped preferences:** Idiosyncratic preferences

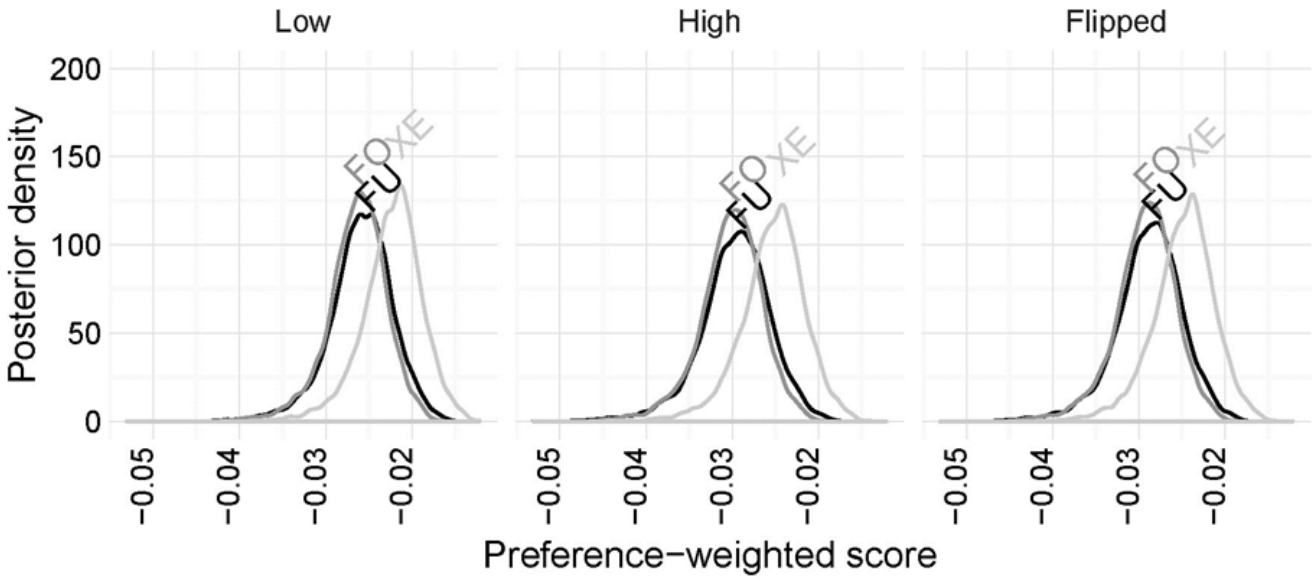


Posterior probabilies of PWOS

Unweighted



Time-weighted



IV. Simulation study of more preference-sensitive setting

For each individual in the simulated population, generate:

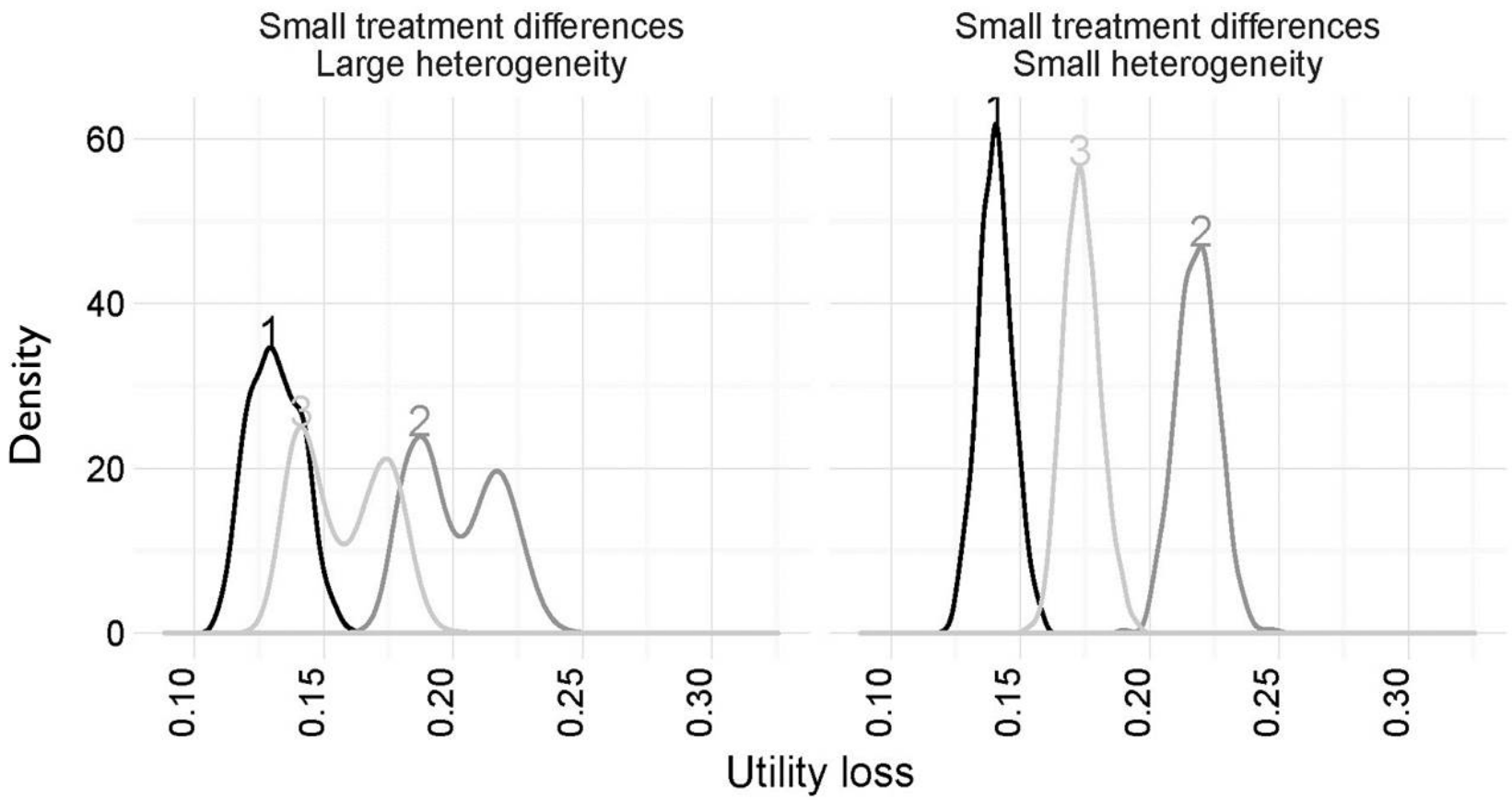
- Vector of correlated true counterfactual outcomes under each treatment
- Vector of correlated predicted outcomes under each treatment
- Latent preference profile class membership
- Vector of correlated individual utilities centered around class mean utilities

Evaluating performance of several versions of PWOS for treatment assignment

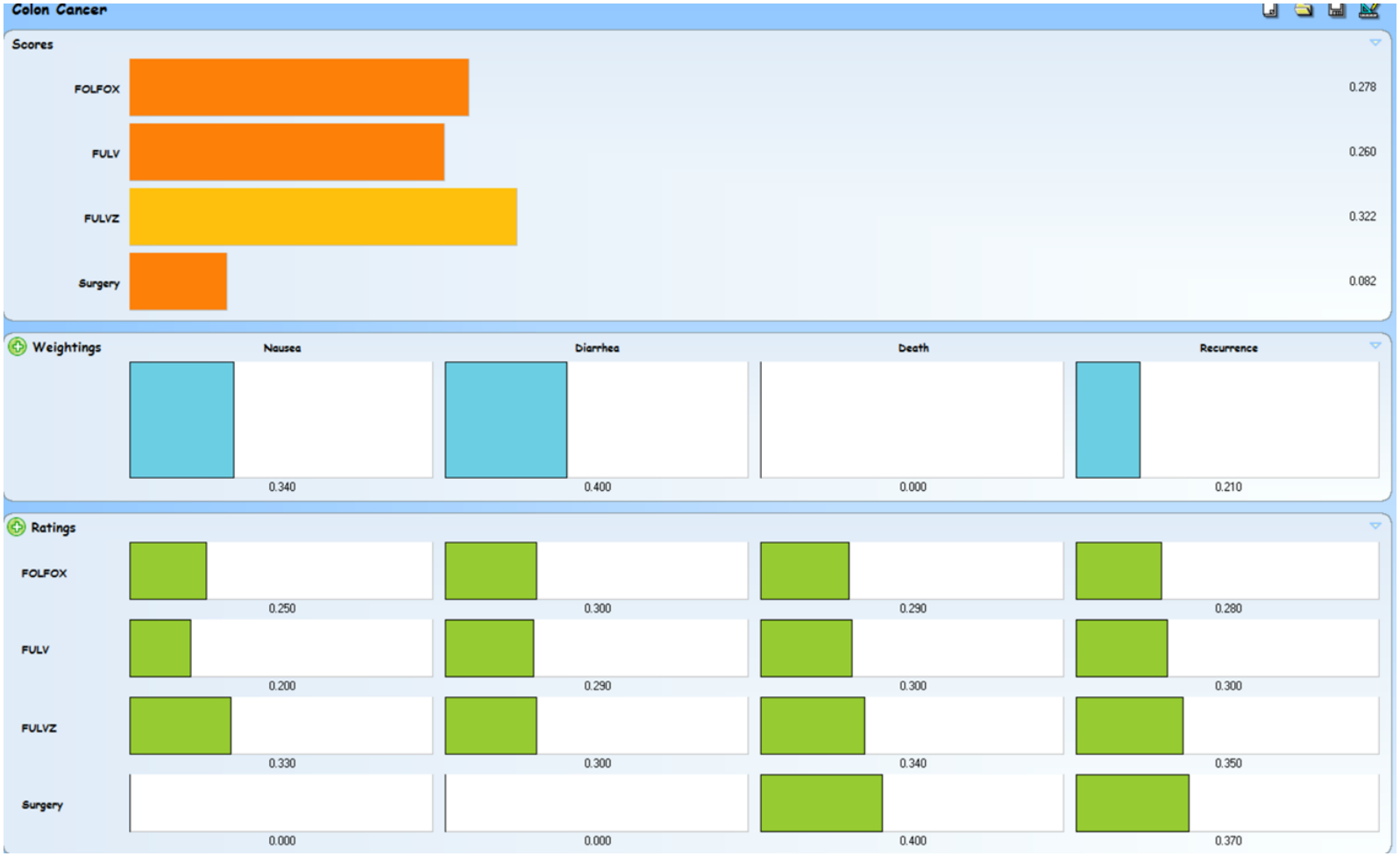
- "Gold-standard" = time-weighted PWOS based on true outcomes and individual's utility values
- In practice treatment decisions based on predicted outcomes
- Considered 3 Decision Rules:
  1. PWOS 1 = predicted outcomes, individual utilities
  2. PWOS 2 = predicted outcomes, pop. average utilities
  3. Global rule = treatment with best average survival in population

Implementing PWOS with personalized data minimizes assignment to suboptimal treatment

Utility loss = difference in PWOS under "gold standard" treatment and PWOS under alternative treatment



Implementing PWOS in a clinical setting



Masya L, Young J, Solomon M, Harrison J, Dennis R, Salkeld G (2009) Preferences for outcomes of treatment for rectal cancer: Patient and clinician utilities and their application in an interactive computer-based decision aid. Diseases of the Colon and Rectum 52(12):1994-2002

Strengths

Expected treatment outcomes

Hierarchical models for multiple RCTs

- improve precision of predicted treatment outcomes
- model correlation across outcomes
- perform joint inference for multiple treatments, outcomes

Preference-weighted outcome score (PWOS)

- formal approach for ranking treatments: weight predicted outcomes by patient preferences and expected duration
- accounts for uncertainty in outcome predictions
- improve allocation of patients to optimal treatment compared global assignment

Weaknesses

Expected treatment outcomes

Hierarchical models for multiple clinical trials

- difficult to specify a joint model for mixed outcome types
- strong assumption of exchangeability across arms
- requires individual patient data

Preference-weighted outcome score (PWOS)

- Our clinical application was not very preference-sensitive
- patient preferences may change over time - utilities assessed at treatment start may not truly be constant
- eliciting patient utilities for all relevant outcomes may not be feasible in all clinical visits

Future directions

- Sensitivity of our methods to correlation across outcomes and uncertainty in predicted outcomes
- Applying PWOS method to more preference-sensitive clinical application
- Extending PWOS method to incorporate time-to-event outcomes rather than categorical

Thank you!

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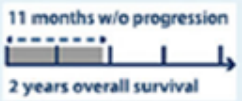
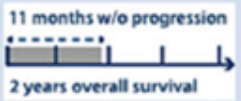
Utilities survey

Characteristic	Treatment A	Treatment B
Time without tumor progression	Medium 	Medium 
Side effect of Skin	Moderate 	None 
Nausea and Vomiting	Mild 	Severe 
Diarrhea	Moderate 	Moderate 
Tiredness/Fatigue	Mild 	Severe 
Tumor related symptoms	Severe 	Mild 
Mode of Administration	Infusion 	Tablet 
	○	○

Muhlbacher A, Bethge S (2015) Patients' preferences: A discrete-choice experiment for treatment of non small cell lung cancer. European Journal of Health Economics 16(6):657-70

Implemented 2 versions of PWOS and universal decision rule

			In practice	
	"Gold Standard"	1. Both personalized	2. Personalized outcome	3. Neither personalized
Outcomes	True counterfactual outcomes	Predicted outcomes	Predicted outcomes	Assign all individuals to treatment with best average survival
Utilities	Individual utility values	Individual utility values	Population average utility values	N/A
Time-weights	Based on true outcomes	Based on predicted outcomes	Based on predicted outcomes	N/A