Joint utility estimators in substance use disorders

By: Eve Wittenberg, Jeremy W. Bray, Achamyeleh Gebremariam, Brandon Aden, Bohdan Nosyk, and Bruce R. Schackman

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Abstract:

Background: Although co-occurring conditions are common with substance use disorders (SUDs), estimation methods for joint health state utilities have not yet been tested in this context. **Objectives:** To compare joint health state utility estimators in SUD to inform economic evaluation. **Methods:** We conducted two Internet-based surveys of US adults to collect community perspective standard gamble utilities for SUD and common co-occurring conditions. We evaluated six conditions as they occur individually and four combinations of these as they occur in tandem. We applied joint utility estimators using the six individual conditions' utilities to compare their performance relative to the observed combination states' utilities. We assessed performance with bias (estimated utility minus observed utility) and root mean square error (RMSE). **Results:** Using 3892 utilities from 1502 respondents, the minimum estimator was statistically unbiased (i.e., the 95% confidence interval included 0) for all combination states that we measured. The maximum estimator was unbiased for two states and the linear index and adjusted decrement estimators were unbiased for one state. The maximum estimator had the smallest RMSE for two combination states (back pain and prescription opioid misuse [0.0004] and injection crack and injection opioid use [0.0007]); the linear index and minimum estimators had the smallest RMSE for one combination state each. The additive and multiplicative estimators had the largest RMSE for all states. **Conclusions:** Our results demonstrate the usefulness of the minimum estimator in this context, and confirm the inadequacy of the additive and multiplicative estimators. Further research is needed to extend these results to other SUD states.

Keywords: cost-utility analysis | preferences | substance use | utility

Article:

Introduction

The increasing prevalence of multiple chronic conditions among individuals of all ages compels health services researchers to better understand the health-related quality of life (HRQOL) of co-occurring illness [1]. About one in four adults and two in three Medicare beneficiaries have multiple chronic conditions [2], [3]. Co-occurring conditions are particularly common among individuals with substance use disorders (SUDs): approximately 39% of adults in the United States who have an SUD also have a mental health disorder [4], and 50% to 80% of injection drug users are infected with both HIV and the hepatitis C virus [5]. Because the incidence of opioid use disorder is increasing dramatically [6], understanding the HRQOL of opioid use disorder, its treatment, and co-occurring conditions is critical to decisions about optimal intervention.

Comparative effectiveness research, including cost-utility analysis (CUA) and cost-effectiveness analysis (CEA), is useful to inform decision making. CUA and CEA use quality-adjusted life-years (QALYs) as the outcome measure to quantify benefits accrued by an intervention or treatment relative to costs. QALYs are a function of the quality and longevity of a person's life; they are the products of the HRQOL for a particular health state and the number of years lived in that state. HRQOL is measured via health state utilities, which are an economic concept that quantifies HRQOL on a uniform scale so that it is comparable across conditions [7]. Simultaneously occurring conditions present challenges for CUA and CEA because we do not fully understand how having two (or more) conditions at the same time affects HRQOL. We therefore have difficulty predicting the health state utilities and QALYs that accompany an intervention or treatment directed toward one condition in someone with multiple conditions—we do not know how the utility resulting from the second (or third) condition may change, or not, by one being resolved [8]. Because of the sheer volume of possible simultaneously occurring health conditions, mechanisms for combining health state utilities for individually occurring conditions into multiple-state utilities would be highly useful for CEA and CUA [8].

Recent literature has posited methods of estimating multiple-state utility from the constituent individual ("single") states—that is, taking known utilities for individual states and mathematically combining them to arrive at a utility for the combination state [9]. Such methods are commonly called "joint utility estimation." Simultaneously occurring health states can take many forms in how they affect an individual. They can vary from being independent, meaning the experience of one has no effect on the experience of the other, to being interdependent, meaning the experience of one affects the experience of the other. For most co-occurring conditions, one likely ameliorates or exacerbates the experience of the other to some degree. Conditions that are physiologically unrelated, such as blindness and breast cancer, are likely experienced only minimally differently when they co-occur than when they are experienced individually. Breast cancer has little effect on the experience of blindness and vice versa. Nevertheless, conditions that are physiologically related, such as opioid use disorder and chronic pain, are likely experienced very differently when they co-occur. Pain is alleviated by opioids and so it is ameliorated in the presence of opioid use disorder and would have a better HRQOL than when experienced alone. Estimating joint utilities is therefore a complicated task that involves assumptions about individuals' experiences.

The literature has proposed five options for estimating joint health state utility from single state utility. Methods have been assessed on the basis of their mathematical accuracy in predicting observed joint state utility from observed single state utility. More recent literature has attempted to incorporate psychological mechanisms to explain the relationship between the two. The five options are as follows: 1) the minimum estimator, in which the lesser of two single states' utilities is used as an estimate of their joint utility; 2) the additive, or constant decrement estimator, in which the sum of the two single states' disutilities (i.e., 1− utility) is subtracted from perfect health (1.0) to estimate their joint utility (to a minimum of 0); 3) the multiplicative estimator, in which the product of the two single states' utilities is used as an estimate of their joint utility [10]; 4) the "linear index estimator," a parametric model that uses the weighted sum of the minimum and the maximum of the two single states' utilities and their interaction to estimate their joint state utility [11]; and 5) the "adjusted decrement estimator," a nonparametric model that combines the two single states' utilities in proportion to the difference between them [12].There is a lack of consensus on the best estimator among this list and research has shown conflicting results [9]. We conducted this study to assess the accuracy of joint health state utility estimators in the context of SUDs, a case in which co-occurring conditions are common and none of these estimators has been tested. Our goal was to inform the estimation of utility scores for use in economic evaluation of SUD treatments and interventions.

Methods

Study Design

We conducted a series of two cross-sectional, Internet-based utility surveys of a representative panel of the US adult, noninstitutionalized population (the GfK Knowledge Panel [13]) from December 2013 to January 2014 and from March to April 2015. We administered the identical surveys to a randomly selected sample of the panel at these two time points, varying only the health states that were evaluated. We elicited community perspective utilities by asking a sample of the general population to evaluate hypothetical health state descriptions, following accepted practice [7]. We asked each respondent to evaluate between three and six randomly assigned hypothetical health state descriptions describing SUD, common co-occurring conditions (depression and chronic pain), polysubstance use, and SUD and co-occurring conditions occurring simultaneously. We estimated community perspective utilities because of their usefulness for economic evaluation [7], [14], and used direct elicitation methods to avoid the need for recruiting patients with these conditions as is required in indirect utility assessment [15] (direct measures ask a sample of the general population to evaluate hypothetical health state descriptions that they may or may not have personally experienced; indirect measures ask a sample of individuals with a particular condition to complete an assessment instrument to which population utilities are assigned [7]). Utility data from the two surveys were combined to create the analytic data set (Fig. 1); complete results from the first survey are reported elsewhere [16].

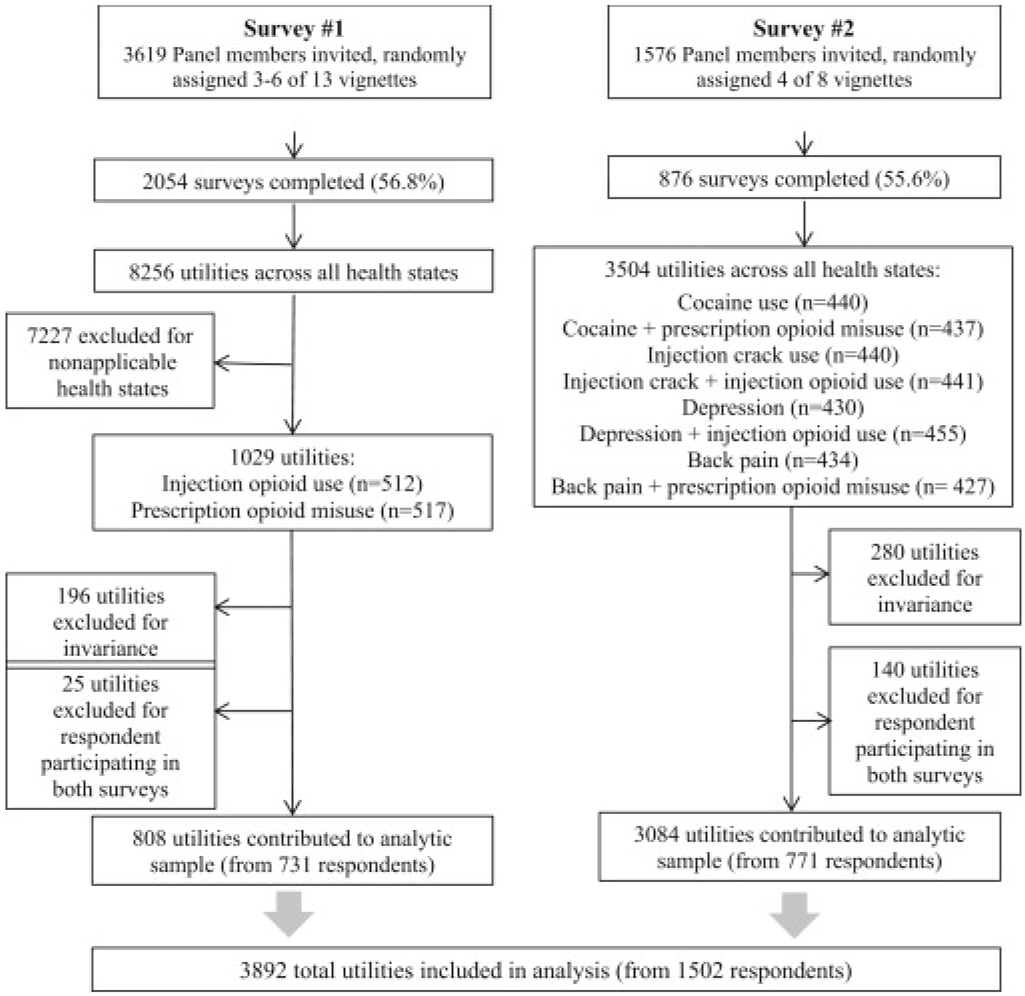

Fig. 1. Data sources for analytic sample.

For both surveys, respondents evaluated their own current health as a practice exercise before evaluating the hypothetical health states, and provided basic demographic information at the end (which was supplemented with additional demographic data provided by the survey research firm). A 100-point rating scale was used as a warm-up before standard gamble (SG) evaluations [7]. The SG technique typically asks respondents to choose between living in a described (hypothetical) health state for the rest of their life and accepting a “gamble” that includes a chance of death and a chance of living in perfect health. The chance of death and perfect health in the gamble are varied until the point that the respondent is indifferent between living in the described health state and taking the gamble [7]. We used visual aids to help respondents comprehend probabilities (dot matrices). Respondents finished the gamble exercise after multiple iterations when a desired level of precision was reached for the indifference point (0.01 utility for our surveys), or if they toggled back and forth between the same two values 3 times. They could also indicate indifference by selecting a response button labeled “too hard to choose.” A respondent could choose a button “I know my answer” to avoid the iterative chance presentation process, and type in a value between 0% and 100%. Error messages were presented on the screen if a respondent selected a potentially illogical response, with an option to revise the answer (e.g., choosing to take a pill with 100% chance of death and 0% chance of perfect health, which is tantamount to selecting suicide in the face of a described health state) [17].

We followed established practice in developing the hypothetical health state descriptions [18]: for the first survey, we collected qualitative data from individuals in substance abuse treatment programs and combined them with data from the literature and expert opinion; for the second survey, we used data from the literature and expert opinion [16]. All health state descriptions were reviewed by clinical practitioners and refined by the investigators before inclusion in the survey. All included similar domains and were of similar length; none was identified by name to respondents. We included a total of 10 health states in our analysis: injection opioid use, prescription opioid misuse, cocaine use, injection crack use, chronic back pain, and moderate depression, plus the simultaneously occurring states of cocaine and prescription opioid misuse, injection crack and injection opioid use, back pain and prescription opioid misuse, and depression and injection opioid use. The simultaneously occurring states were described as one hypothetical state that an individual was experiencing, with all characteristics that would exist when the simultaneous states co-occur. Injection opioid use and prescription opioid misuse were evaluated in the first survey and the rest in the second survey (Fig. 1; all health state descriptions are included in the Appendix in Supplemental Materials found at doi:10.1016/j.jval.2016.09.2404).

The sample sizes for the surveys were designed to detect meaningful differences in mean values between health states on the basis of existing estimates of values for similar health states using similar measures [19]. Minimally important differences in utilities across measurement techniques and conditions range from 0.03 to 0.07 [20], [21]. We sought a sample of approximately 425 to 475 responses per health state to detect these differences on the basis of conservative assumptions about variation in observed means.

Statistical Analysis

We created an analytic data set that excluded responses that failed invariance criteria, which were defined as those responses in which all SG responses from a respondent including the practice question were the same and equal to 0 (the minimum), 0.5 (the starting point for the exercise), or 1.0 (the maximum) [17]. We also excluded utilities in both surveys provided by respondents who by chance participated in both. We calculated means and 95% confidence intervals for the SG utilities for all states. We calculated the predicted utility for the joint states using five joint health state estimators described in the literature (additive, multiplicative, minimum, linear index, and adjusted decrement) and one that we hypothesized to be relevant in this context (maximum), and descriptively compared each with the directly measured utility for each joint health state using measures reported in the literature (bias and root mean square error [RMSE]) [9]. We used 1000 bootstrap iterations to estimate the bias (defined as the predicted mean using the estimator minus the observed mean) and the RMSE (defined as the square root of the mean of the square of all errors between predicted and observed utilities) for the joint state estimators relative to the observed joint state utilities, and calculated the 95% confidence interval for the bias and the interquartile range for the RMSE. Finally, we visually depicted the bias for each estimator with bias density curves showing the dispersion of the bootstrapped estimates. This graphing technique allows for comparison among estimators relative to a 0 bias line and indicates the precision of each estimator (i.e., curves further from 0 bias indicate larger bias and those broader in span indicate less precision). Analyses were conducted using Stata version 12

(StataCorp, College Park, TX); graphs were made using Microsoft Excel.The study was approved by the Harvard T.H. Chan School of Public Health and Weill Cornell Medicine institutional review boards.

Results

A total of 876 respondents completed the second survey, providing 3504 utilities for eight health states (55.6% completion rate; Fig.1). After excluding invariant responses (n = 280) and utilities received from those respondents who participated in the first survey as well (n = 140), we had 3084 utilities from 771 respondents for the analytic sample. We combined these with 808 utilities from 731 respondents from the first survey (after exclusions for invariant responses [n = 196] and utilities from respondents who participated in both surveys [n = 25]),for a total of 3892 utilities from 1502 respondents for analysis.

About half of the respondents in both surveys were female, nearly three-quarters were white, more than 60% were married, and more than half had completed at least some college education and were employed (Table 1). Utilities for all health states are presented in Table 2, and they ranged from 0.555 to 0.714. Comparing the directly measured utilities for the joint states with their constituent individually occurring states, the mean utility for the cocaine use and prescription opioid misuse state was lower than that of each individually occurring state, whereas the mean utility for the moderate depression and injection opioid use state was between that of the two individually occurring states. The mean utilities for the remaining joint states (injection crack use and injection opioid use, chronic back pain and prescription opioid misuse) were both higher than the utilities for their constituent, individually occurring states.

The prediction methods underestimated the directly measured joint health state utilities 83% of the time (20 out of 24 predictions by six predictors for four health states; Table 3). The bootstrapped bias and RMSE for all estimators are presented in Table 4. The minimum estimator's 95% confidence intervals for bias included 0 for all four joint states (Fig.2). The maximum estimator's 95% confidence intervals for bias included 0 for two of the four joint states (back pain and prescription opioid misuse, injection crack use and injection opioid use), and the linear index and the adjusted decrement estimators' 95% confidence intervals for bias included 0 for one state (cocaine use and prescription opioid misuse). The RMSE was the smallest for the linear index estimator for one state (cocaine use and prescription opioid misuse) and for the maximum estimator for two states (back pain and prescription opioid misuse, injection crack use and injection opioid use), and it was negligibly different between the minimum and linear index estimators for the fourth state (depression and injection opioid use). The second smallest RMSE was found for the minimum estimator in three states and for the linear index estimator in one state. The additive and multiplicative estimators had the largest RMSE for all states.

Table 1. Sample characteristics of first and second surveys' complete and analytic samples and US population data

	First survey*				Second survey				
	Complete sample (n=900)		Analytic sample (n=731)		Complete sample (n=839)		Analytic sample (n=771)		US population
Characteristics	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**(%)**
Age (y)									
8–24	83	9.2	69	9.4	75	8.9	72	9.3	6.8†,‡ [24]
5–44	275	30.6	212	29.0	258	30.8	226	29.3	26.5
45–64	350	38.9	284	38.9	328	39.1	303	39.3	26.4
65+	192	21.3	166	22.7	178	21.2	170	22.1	13.8
Education									
Less than high school	83	9.2	67	9.2	66	7.8	58	7.5	13.7 [25]
High school	294	32.7	239	32.7	245	29.2	216	28.0	28.0
Some college	244	27.1	197	27.0	248	29.6	230	29.8	31.3
Bachelor's degree or higher	279	31.0	228	31.2	280	33.4	267	34.6	27.0
Race/ethnicity									
White NH	669	74.3	550	75.2	604	72.0	566	73.4	62.8 [24]
Black NH	78	8.7	62	8.5	85	10.1	71	9.2	12.2
Other NH	54	6.0	41	5.6	73	8.7	66	8.6	25.0
Hispanic	99	11.0	78	10.7	77	9.2	68	8.8	16.9
Sex, male	442	49.1	352	48.2	430	51.3	396	51.4	49.2 [24]
Marital status									
Widowed/separated/divorced/ never married	345	38.3	281	38.4	289	34.5	265	34.4	49.7 [26]
Married/living with partner	555	61.7	450	61.6	550	65.6	506	65.6	50.3§
Household annual income (US $)									
<25,000	174	19.3	135	18.5	161	19.2	140	18.2	24.0 [27]
25,000–49,999	201	22.3	158	21.6	163	19.4	151	19.6	23.0
50,000–99,999	290	32.2	236	32.3	281	33.5	258	33.5	29.0
100,000+	235	26.1	202	27.6	234	27.9	222	28.8	24.0
Employed at present	502	55.8	406	55.5	485	57.8	446	57.9	59.6‖ [28]

Note. Percentages may not sum to 100 because of rounding.
NH, non-Hispanic.
* Survey respondents who provided utilities for states used in this analysis. Complete sample characteristics reported previously [16].
† Ages 20–24 y.
‡ Age proportions of entire US population.
§ Includes married only, excluding living with partner.
‖ Civilian population.

Table 2. Directly measured SG utilities for single states and joint states: Mean, SE, and 95% CI

Health state	**n**	**Mean**	**SE**	**95% CI**
Cocaine use	380	0.714	0.015	0.685–0.743
Prescription opioid misuse	406	0.680	0.015	0.652–0.709
Cocaine and prescription opioid misuse	382	0.647	0.016	0.615–0.679
Injection crack misuse	394	0.582	0.017	0.548–0.615
Injection opioid use	402	0.555	0.017	0.523–0.588
Injection crack and injection opioid use	384	0.597	0.017	0.563–0.631
Moderate depression	383	0.672	0.015	0.643–0.702

Health state	n	Mean	SE	95% CI
Injection opioid use	402	0.555	0.017	0.523–0.588
Moderate depression and injection opioid use	402	0.594	0.017	0.562–0.627
Chronic back pain	382	0.664	0.015	0.634–0.693
Prescription opioid misuse	406	0.680	0.015	0.652–0.709
Chronic back pain and prescription opioid misuse	377	0.687	0.015	0.657–0.716

CI, confidence interval; SE, standard error; SG, standard gamble.

Table 3. Directly measured and predicted joint health state utilities for six alternative estimation methods, and whether estimation overpredicted or underpredicted directly measured utility: Minimum, maximum, additive, multiplicative, linear index estimator, and adjusted decrement estimator

Joint health state	Directly measured	Minimum	Maximum	Additive	Multiplicative	Linear index	Adjusted decrement
Cocaine and prescription opioid misuse	0.647	0.680↑	0.714↑	0.394↓	0.485↓	0.642↓	0.618↓
Injection crack and injection opioid use	0.597	0.555↓	0.582↓	0.137↓	0.323↓	0.525↓	0.452↓
Depression and injection opioid use	0.594	0.555↓	0.672↑	0.228↓	0.373↓	0.548↓	0.475↓
Back pain and prescription opioid misuse	0.687	0.664↓	0.680↓	0.344↓	0.451↓	0.622↓	0.592↓

Note. ↑ = estimator overpredicted observed joint utility and ↓ = estimator underpredicted observed joint utility.

Table 4. Comparison of different estimators for predicting joint health state utilities in terms of bias (and SD and 95% CI) and RMSE (and IQR)

Estimator	Bias	SD	95% CI	RMSE	IQR
Cocaine and prescription opioid misuse					
Minimum	0.033	0.023	−0.011 to 0.077*	0.0016	0.018 to 0.049
Maximum	0.066	0.022	0.023 to 0.110	0.0051	0.052 to 0.083
Additive	−0.253	0.028	−0.308 to −0.199	0.0642	−0.272 to −0.233
Multiplicative	−0.162	0.023	−0.207 to −0.117	0.0263	−0.176 to −0.145
Linear index	−0.006	0.020	−0.045 to 0.034*	0.0004	−0.018 to 0.009
Adjusted decrement	−0.029	0.024	−0.077 to 0.018*	0.0014	−0.045 to −0.012
Injection crack and injection opioid use					
Minimum	−0.041	0.023	−0.087 to 0.004*	0.0024	−0.059 to −0.027
Maximum	−0.015	0.024	−0.061 to 0.031*	0.0007	−0.030 to 0.002
Additive	−0.459	0.030	−0.518 to −0.401	0.2124	−0.480 to −0.440
Multiplicative	−0.274	0.022	−0.317 to −0.230	0.0756	−0.288 to −0.258
Linear index	−0.071	0.021	−0.112 to −0.031	0.0057	−0.087 to −0.058
Adjusted decrement	−0.145	0.024	−0.192 to −0.097	0.0220	−0.162 to −0.129
Depression and injection opioid use					
Minimum	−0.039	0.023	−0.084 to 0.006*	0.0020	−0.054 to−0.023
Maximum	0.078	0.023	0.034 to 0.122	0.0067	0.063 to 0.095
Additive	−0.367	0.028	−0.421 to −0.312	0.1345	−0.385 to −0.346
Multiplicative	−0.221	0.022	−0.263 to −0.179	0.0490	−0.235 to −0.206
Linear index	−0.046	0.020	−0.085 to −0.007	0.0025	−0.059 to −0.033
Adjusted decrement	−0.120	0.024	−0.166 to −0.074	0.0148	−0.135 to −0.103
Back pain and prescription opioid misuse					
Minimum	−0.023	0.020	−0.063 to 0.017*	0.0012	−0.040 to −0.013
Maximum	−0.007	0.020	−0.046 to 0.033*	0.0004	−0.018 to 0.009
Additive	−0.343	0.026	−0.394 to −0.292	0.1192	−0.362 to −0.327

Estimator	Bias	SD	95% CI	RMSE	IQR
Multiplicative	−0.235	0.021	−0.276 to −0.194	0.0564	−0.250 to −0.222
Linear index	−0.065	0.019	−0.102 to −0.029	0.0049	−0.079 to −0.055
Adjusted decrement	−0.095	0.022	−0.138 to −0.051	0.0101	−0.112 to −0.083

CI, confidence interval; IQR, interquartile range; RMSE, root mean square error.

* 95% CI includes 0.

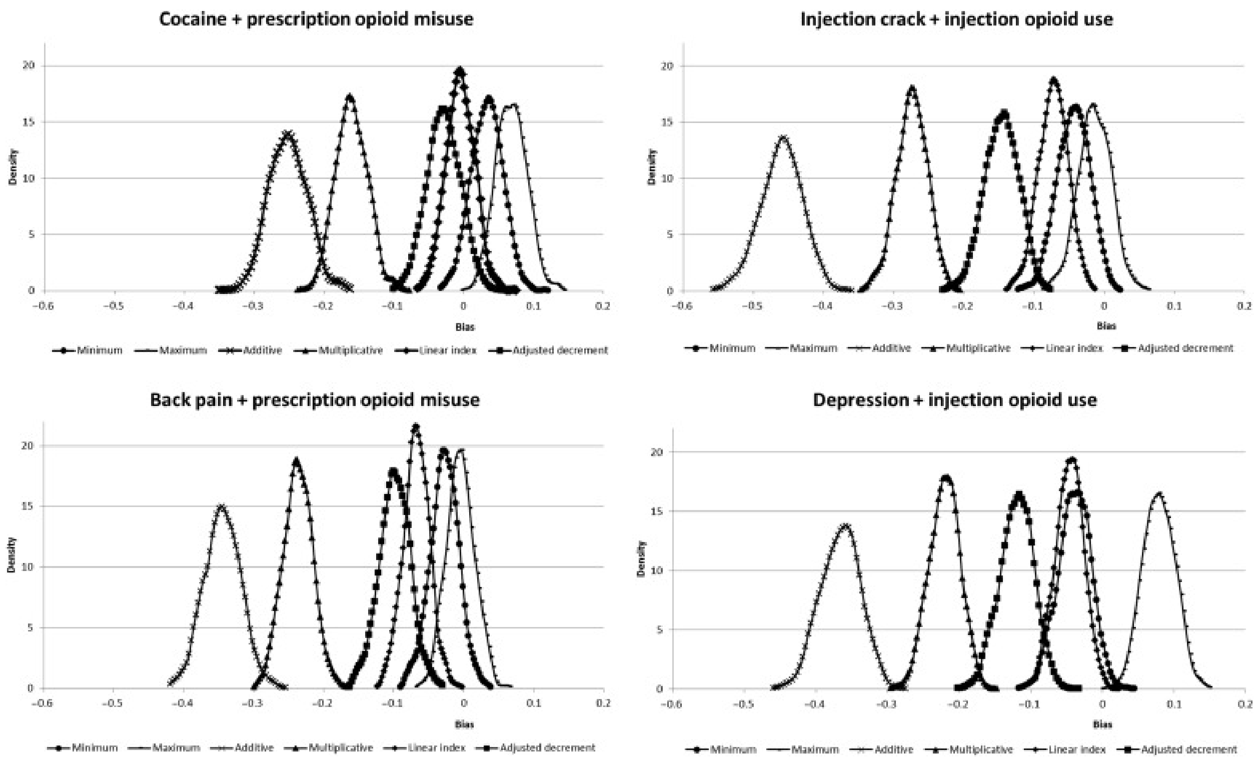

Fig. 2. Bias density graphs across joint health state utility estimators. Bias is the estimated utility minus observed utility, using bootstrapped estimator distribution. Zero bias indicates a more accurate estimator. Negative bias indicates that the estimator underestimated the observed utility, whereas positive bias indicates that the estimator overestimated the observed joint utility.

Discussion

In our data set, the utility of combination health states describing polysubstance use and opioid use disorder in conjunction with common co-occurring conditions followed no clear pattern relative to their constituent single states: they were evaluated at higher, lower, in between, and of equal utility to the single states. Of the available joint health state utility estimators, the minimum estimator performed the best across the entire group, showing bias that was statistically nonsignificantly different from 0 for all four combination states. Other estimators performed better than the minimum estimator in some of our joint health states, but none had its consistent lack of statistically significant bias. The additive and multiplicative joint utility estimators performed consistently the worst of those available, showing bias for all four states.

Utility estimation can be time-consuming and complex [7]. It is helpful for both users and consumers of utilities to have estimation methods that are transparent and accessible. The volume of health states describing individually occurring conditions is vast, and when co-occurring conditions are added the number increases exponentially. Utility estimation for all such states is untenable, and so methods to arrive at joint state utilities from their constituent single states are immensely useful to economic evaluation. Five methods of joint state utility estimation have been proposed in the literature, from simple addition to more complex models [9]. Criteria for assessing their usefulness prioritize accuracy in prediction, and specifically minimizing bias, although psychological underpinnings have also been considered relevant [8]. The literature to date is inconclusive about the recommended approach. A recent review recommended the multiplicative estimator [9], although others have supported the minimum estimator [10], a linear combination model [11], and an adjusted decrement model [12]. Although most studies of joint state utilities focus on community perspective values, as is recommended for use in economic evaluation [14], the literature has assessed approaches using both indirect and direct utility elicitation methods, a range of diseases and conditions, various definitions of what constitutes a joint health state, and multiple criteria for comparison across methods [9]. We opted to collect community perspective utilities from a US population sample to enable economic evaluation following recommended guidelines [14], and used direct utility elicitation because of the practical difficulties of collecting indirect utility estimates from representative samples of active opioid users with or without co-occurring conditions. Our definition of joint utilities is context-specific for SUDs: we identified individual health conditions that commonly occur together and considered these joint states. Some investigators have used approaches similar to ours, such as in prostate cancer [11], whereas others have considered two states that are simply recorded as prevalent together in population data sets (such as the Medical Expenditures Panel Survey [12]). The variability in conclusions about estimators' usefulness may be due to these differences, which calls for context-specific use—meaning some estimators perform the best in some disease contexts, and some measurement methods are better in other contexts.

The SUD context provides an illustration of utility interaction that has implications for our results. Our joint states combined conditions commonly seen in SUDs that are genuinely co-occurring conditions but may also interact from a utility perspective. For example, prescription opioid misuse and chronic pain independently result in diminished utility, but when experienced together opioid misuse may improve the utility of chronic pain, because opioids diminish pain. Similarly, injection opioid use may temporarily offset diminished health utility from depression when experienced in combination, whereas both conditions have utility decrements when experienced independently. In these situations, we find it plausible that the utility for either single state could in fact be worse than the utility for them together, because one may moderate the other. The maximum estimator could reasonably perform well for these joint states, disputing the assumption that joint state utilities must by definition be lower than either constituent single state (which some have termed "logically inconsistent" [22]).

Opioid misuse may be unique in that opioids when properly used can increase utility by mitigating pain. Misuse is accompanied by deterioration in quality of life and therefore a utility decrement. But in combination with other conditions such as back pain or depression as we studied, there are multiple effects at play: opioid misuse decreases utility, as does pain and depression, but the co-occurrence may mitigate effects. Our combination states of opioid misuse and these conditions had utilities in one case between the two individual states' utilities and in the other the same as one of the two. We speculate that there was a mitigation effect occurring in these joint states that ameliorated the negative quality of life effect of the individual states. In contrast, our polysubstance use states including opioid misuse had combination state utilities that were in one case below either single state and in the other case above both single states. The explanation of these polysubstance joint state utilities is unclear and requires further study.

It is important to note some limitations in our study. First, the SG is the gold standard for utility elicitation but has limitations—it is subject to respondent misunderstanding, and as with all direct elicitation methods, it is contingent on the accuracy and veracity of the hypothetical health states [7].We exerted great care and thoughtfulness in designing our health state descriptions to accurately reflect the experience of the individual and joint states, but they are simplifications of reality. Importantly, our joint states represent the interaction between opioid use and co-occurring conditions, such that pain with opioid misuse was experienced as less severe than pain in the absence of opioids, as would be expected in their simultaneous occurrence. We excluded about 11% of our data for invariance, which is a substantial but unremarkable rate for SG surveys [17].Second, we administered our survey online, which is known to produce results different from face-to-face administration for some direct utility elicitation methods [23]. Although in-person administration is ideal, online administration allowed us to access a national sample of respondents within our budget constraint, which is a strength of our study. It is unlikely that mode effects are different for individual and joint state utilities, and so confining our analysis to comparisons of single and joint state utilities collected with one mode of administration may diminish the risk of bias in our results. That said, an ideal replication would use different modes to compare results. Third, we combined data from two surveys. The second survey was administered, however, with attention to consistency to allow for precisely the analysis that was conducted. We attained some protection from bias by the surveys being identical except for the health states that were evaluated, the sample for each being randomly selected from the same panel (with duplicate respondents excluded), and the time between surveys being relatively short. Fourth, we collected utilities for only four joint health states within the SUD context, and so the external validity of our results is limited. Finally, we used only two measures of performance for joint estimators—bias and RMSE—and did not attempt to reconcile differences between them when they arose or examine any patterns in respondent characteristics (or other variables) that may affect the performance of the estimators. Further research is warranted to extend our work in these areas—to additional joint states in SUD, to potential differences within populations that could be leveraged to improve estimation methods, and to further characteristics of estimators that would reveal optimal performance.

Conclusions

In the states we assessed, the minimum estimator performed well—it was most often unbiased, providing the most accurate estimate of joint state utility. We found no evidence to support the additive or multiplicative estimators because these performed the worst of those available—they were the most biased, providing the least accurate estimates of joint state utility. Further research will advance our knowledge of combining single state utilities to understand co-occurring conditions and whether these results are unique to SUDs or to the states we assessed. The simplicity, transparency, and accessibility of the minimum estimator are compelling rationales to consider this approach when joint SUD utilities are not empirically available.

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