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ORIGINAL RESEARCH

Impact of Financial Considerations on Willingness to Take Sacubitril/Valsartan for Heart Failure

Birju R. Rao, MD; Candace D. Speight, MPH; Larry A. Allen, MD, MHS; Scott D. Halpern, MD, PhD; Yi-An Ko, PhD; Daniel D. Matlock, MD, MPH; Miranda A. Moore, PhD; Alanna A. Morris, MD, MSc; Laura D. Scherer, PhD; Mary C. Thomson, BA; Peter Ubel, MD; Neal W. Dickert, MD, PhD

BACKGROUND: Sacubitril/valsartan improves health outcomes for heart failure with reduced ejection fraction relative to angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, but it carries higher out-of-pocket costs. Neither the impact of cost nor how to integrate cost into medical decisions is well studied.

METHODS AND RESULTS: To evaluate the impact of out-of-pocket costs and a novel cost-priming intervention on willingness to take sacubitril/valsartan for heart failure with reduced ejection fraction, participants with self-reported heart disease were surveyed using the online Ipsos Knowledge Panel. Participants were presented with a modified decision aid for sacubitril/valsartan and then, in a 3×2 factorial design, randomly assigned to 1 of 3 cost conditions ($10, $50, or $100/month) and to a control group or cost-priming intervention, defined by being asked questions about their financial situation before learning about the benefits of sacubitril/valsartan. Of the 1013 participants included in the analysis, 85% of respondents were willing to take sacubitril/valsartan at $10, 62% at $50, and 33% at $100 ($P$<0.0001). In a multivariable logistic regression model, participants were more likely to take sacubitril/valsartan at $10 versus $100 (odds ratio [OR], 14.3 [95% CI, 9.4–21.8]) and $50 compared with $100 (OR, 3.6 [95% CI, 2.5–5.1]). Overall, participants in the cost-primed group were more willing to take sacubitril/valsartan than those not primed to consider their financial situation (63% versus 56%, P=0.04). There was no statistically significant interaction between cost conditions and cost priming. Perceived benefit of sacubitril/valsartan over angiotensin-converting enzyme inhibitors or angiotensin receptor blockers decreased as cost increased but did not vary by cost priming.

CONCLUSIONS: Commonly encountered out-of-pocket costs of sacubitril/valsartan may impact individuals' willingness to take the medication even when recommended by their physicians. Priming individuals to consider personal finances before learning about the drug increased willingness to take sacubitril/valsartan.

Key Words: guideline-directed medical therapy ■ heart failure ■ out-of-pocket cost

Heart failure with reduced ejection fraction (HFrEF) affects about 6.5 million adults in the United States and has the highest projected increase in prevalence of any cardiovascular disease over the next decade.[1,2] For years, guideline-directed medical therapy for HFrEF was composed of inexpensive generic medications. In recent years, the therapeutic armamentarium for HFrEF has grown to include the angiotensin receptor-neprilysin inhibitor sacubitril/valsartan and sodium glucose like transporter-2 inhibitors, both of which reduce mortality and morbidity.[3,4] However, these newer medications have higher out-of-pocket

See Editorial by Kittleson

Correspondence to: Birju R. Rao, MD, Emory University School of Medicine, 1462 Clifton Way NE, Suite 503, Atlanta, GA 30322. Email: birju.r.rao@emory.edu

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CLINICAL PERSPECTIVE

What Is New?

- Out-of-pocket costs impact patients' willingness to take sacubitril/valsartan over an angiotensin-converting enzyme inhibitor or angiotensin receptor blocker.
- Regardless of out-of-pocket costs, individuals reported a low perceived benefit of sacubitril/valsartan compared with angiotensin-converting enzyme inhibitors or angiotensin receptor blockers.

What Are the Clinical Implications?

- Marked cost sensitivity across a range of typical copay amounts suggests that clinicians need to integrate out-of-pocket costs into decisions.
- Priming patients to consider their financial situation may impact willingness to take medications and warrants further evaluation as a strategy for approaching these cost discussions.

Nonstandard Abbreviations and Acronyms

HFrEF	heart failure with reduced ejection fraction
OOP	out-of-pocket

(OOP) costs. The average annualized OOP costs for patients with Medicare Part D coverage is $1685 for sacubitril/valsartan ($1400 more than the cost of an angiotensin receptor blocker alone),[5] $1615 for dapagliflozin,[6] and $1097 for empagliflozin.[7]

Discussion about cost is often absent from decision making between clinicians and patients.[8] The reasons are multiple and range from unavailability of cost information to clinicians' discomfort with talking about medical care in a way that puts a price on patients' welfare or longevity.[9] However, patients with HFrEF face real decisions about whether to take more effective medications at the expense of greater financial burden.[10] Financial hardship is not a trivial concern; it has been shown to result in avoidance of care and medication nonadherence, and choosing to pay for medication may involve foregoing other things (medical or not) that patients value.[11–13] In patients with HFrEF, lower income has also been associated with poorer outcomes.[14] Consideration of OOP costs should be part of shared decision making, but contextualizing expected benefits of a medication relative to its cost can be challenging for patients. In the case of HFrEF, medications are associated with absolute reductions in mortality (2%–3% over 2 years) that patients may be quick to dismiss despite being clinically significant. It may be reasonable for some patients to forego this benefit for financial reasons, but proper contextualization of medical and financial implications is important.

Integrating cost discussions into shared decision-making for HFrEF requires greater understanding about how patients make cost–benefit tradeoffs and how choices are impacted by presentation of OOP costs. One small study suggested cost sensitivity among patients with HFrEF,[8] but little is known about the impact of different OOP costs on patients' choices of HFrEF medications. How financial considerations are discussed likely matters as well. Contextualizing costs by priming patients to consider their personal financial situation before presenting OOP costs and medical benefits may impact patients' choices. For instance, patients exposed to a medication cost decision after considering their own financial situation may value the medication differently and focus more on cost implications.

METHODS

Objective

We conducted an experimental survey to assess: (1) willingness of patients with cardiac disease to take sacubitril-valsartan at 3 commonly encountered OOP costs; (2) how priming patients to consider their financial situation impacts their willingness to take sacubitril-valsartan: and (3) the impact of cost and cost priming on patients' perceptions of the benefit of the drug. Data from this study will be made available upon request.

Participants and Study Design

This study was conducted during July 2020 using the Ipsos KnowledgePanel, a nationally representative, online survey panel. KnowledgePanel uses probability-based sampling techniques for recruitment based on home address and provides participants internet access via a tablet if needed; it is more robust and less susceptible to non–probability sampling errors than other internet panels.[15,16] To focus on patients with relevant medical experience, eligible participants included adults who had previously self-identified as having been diagnosed with a heart attack, heart disease, or other heart condition. The nature of their cardiac disease was not further specified. Payment for completing the survey was administered through Ipsos according to their standard practice. This study was deemed exempt from review by the Emory University Institutional Review Board, and completion of the survey was taken to indicate consent for participation.

This experimental study used a 3×2 factorial design (Figure 1). Survey participants were randomized to 1 of 3 OOP cost conditions for sacubitril/valsartan

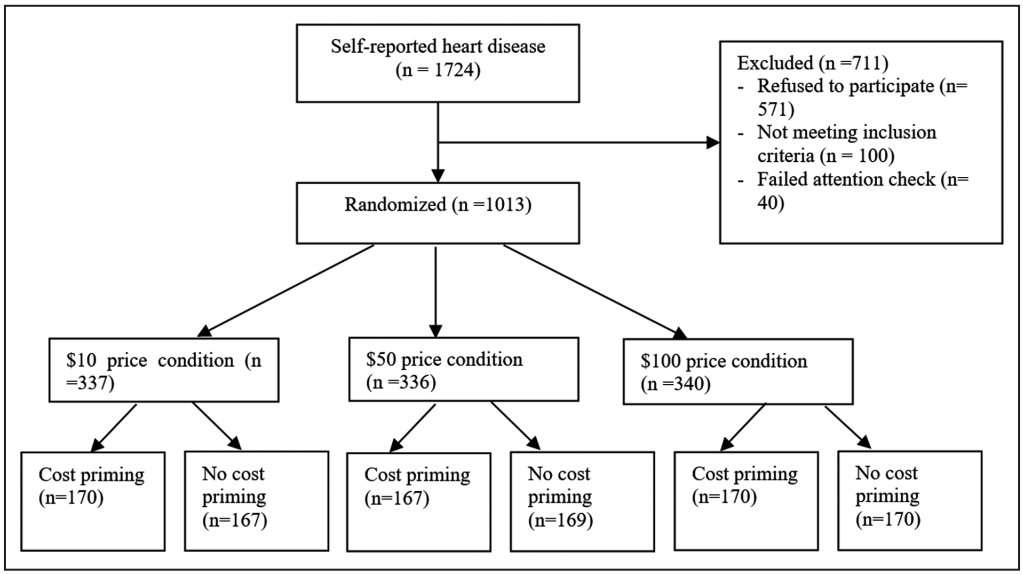

Figure 1. Consolidated Standards of Reporting Trials diagram.

($10, $50, and $100 monthly) representing commonly encountered copayments. The $10 cost condition is common for Americans with commercial insurance who use the manufacturer's patient support program.[17] The $50 cost condition most closely resembles the average copay of sacubitril/valsartan for patients with Medicare Part D, though there is significant variation between plans (and within plans over a year), and copayments as high as $100 are not uncommon.[5] The list price is over $600 per month. In addition, participants were randomized to either a cost-priming condition or a control. Participants randomized to the cost-priming group were asked to rate statements from the Consumer Financial Protection Bureau's Financial Wellbeing Scale (Table S1) about their own personal financial situation[18] before learning about the medication and its OOP costs (cost primed). The Consumer Financial Protection Bureau's Financial Wellbeing Scale is scored from 0 to 100, with a higher score indicating higher financial wellbeing. The control group was asked these questions at the end of the survey, after learning about the medication and its OOP costs and answering questions about their willingness to take the medication (not cost primed).

Survey Instrument

The survey instrument asked respondents to imagine they had HFrEF and that they were considering whether or not to take sacubitril/valsartan or an angiotensin-converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB). Participants were presented with an abbreviated version of a currently available decision aid for this decision[19] (Figure S1) that described the purpose, benefits, and side effects of taking sacubitril/valsartan for HFrEF compared with an ACE/ARB. Central to the decision aid is a pictographic representation of the absolute mortality benefit (≈3% over 2 years) of sacubitril/valsartan demonstrated in the Angiotensin–Neprilysin Inhibition versus Enalapril in Heart Failure study.[4]

Participants were asked, "If you find out that your insurance covers the newer angiotensin receptor-neprilysin inhibitor medicine and you would need to pay ($10, $50, or $100) per month for it, would you take it if your doctor recommended it?" Response options were either "yes" or "no." Participants' comprehension of sacubitril/valsartan's numeric benefit was measured by asking them to identify the number of lives saved with sacubitril/valsartan compared with an ACEI/ARB, and their perception of the value of the drug was assessed by asking them to rank, on a 10-point Likert scale, "[H]ow much better do you think the angiotensin receptor-neprilysin inhibitor medicine is for patients with heart failure compared with an ACEI/ARB?" Health status was assessed by a single-item health screen,[20] and participants were asked to report the number of daily medications they take. Personal financial status was measured using the Consumer Financial Protection Bureau's Financial Wellbeing Scale, described above (Figure S1).[18] Participants were asked about the degree to which they favored aggressive treatment compared with conservative treatment using the Medical Maximizer-Minimizer Scale.[21] An attention check question was included asking participants what condition sacubitril/valsartan treats. Participants who incorrectly answered this question were excluded from the analysis. Demographic information was obtained from Ipsos.

Three rounds of pretesting were conducted using the Amazon Mechanical Turks (MTurks) platform to ensure comprehension of questions, hypothetical pricing scenarios, and the decision aid. Ipsos conducted an additional round of pretesting to ensure the survey performed appropriately on their platform.

Statistical Analysis

A sample size of 1002 participants (167 completed surveys in each of the 6 groups) provided 80% power to detect a 15% difference in stated willingness to take sacubitril/valsartan between each of the 3 price points, and a 10% difference in willingness to take sacubitril/valsartan based on the presence or absence of cost priming at the $50 and $100 price points, with a 2-sided α level of 0.05.

Descriptive statistics of participants' characteristics and responses to key questions were tabulated and stratified by the 3 cost conditions and 2 cost-priming conditions. χ^2 and ANOVA tests were conducted to assess differences in responses across the 6 survey conditions. Logistic regression model was used to evaluate the impacts of cost and cost priming on individuals' willingness to take the sacubitril/valsartan, adjusting for patient characteristics. The interaction between cost and cost priming was considered. An ordinal logistic regression model was used to examine perceptions of how much better sacubitril/valsartan is than and an ACE or ARB across the 3 cost conditions. Likert scale responses were grouped into 3 levels representing perceptions of the drug as not much better (1–3), somewhat better (4–6), and a lot better (7–10) to focus on meaningful differences in responses among participants.[22] The proportional odds assumption was met with a score test (P=0.3). All analyses were conducted using SAS 9.4 (SAS Institute, Cary, NC). The primary analytic plan was preregistered on AsPredicted.[23]

RESULTS

Of 1724 participants contacted, 1153 completed the survey (66.9% response rate). One hundred participants were excluded because they did not state that they had a heart condition, and 40 participants answered the attention check question incorrectly; there were 1013 complete responses. The median age of participants was 69 years (interquartile range, 59–75 years), 36.3% were women, and 82.4% identified as White. Overall, 36.3% reported "fair" or "poor" health on a single-item health screen, and 51.1% of patients reported taking 6 or more medications daily. Thirty-eight percent of participants reported an annual income of $50 000 or less. The groups were evenly balanced across OOP costs and cost-priming conditions for demographic characteristics, health indicators, and financial status (Table 1).

Willingness to Take Sacubitril/Valsartan

Participants' willingness to take sacubitril/valsartan decreased as OOP costs increased. At the $10 price condition, 85% were willing to take sacubitril/valsartan, compared with 62% among individuals at the $50 price condition and 33% at the $100 price condition ($P$<0.0001, Table 2). Overall, individuals who were primed to consider their personal financial situation prior being told about the drug were more willing to take sacubitril/valsartan than those who were not (63% versus 56%, P=0.04, Figure 2); this was the opposite effect from what was hypothesized. In a model including OOP costs, cost priming, and an interaction term, the interaction between OOP costs and cost priming was not significant (P=0.8).

In multivariable logistic regression (Table 3), participants remained significantly more likely to take sacubitril/valsartan at $10 compared with $100 (odds ratio [OR], 14.3 [95% CI, 9.4–21.8]) and at $50 compared with $100 (OR, 3.6 [95% CI, 2.5–5.1]). In addition, those in the cost-priming group had higher odds of willingness to take sacubitril/valsartan compared with those in the non-primed (OR, 1.4 [95% CI, 1.1–2.0]). Respondents reporting higher income were more willing to take sacubitril/valsartan, as were those with better financial well-being (OR, 1.01 [95% CI, 1.001–1.03]) and with higher medical maximizer scores (OR, 1.3 [95% CI, 1.2–1.5]). In an exploratory subgroup analysis examining the relationship between cost priming and income, the impact of cost priming was isolated to individuals with an income of $75 000 and above (Figure 3). However, the interaction between cost priming and income was not significant (P=0.3).

Sensitivity analysis, excluding people who did not correctly identify the numeric mortality benefit of sacubitril/valsartan, was performed to examine whether these effects were present only among individuals with correct understanding of the numeric benefits of the drug (Figure S2). The relationship between price and willingness to take the medication remained significant (P<0.001) and was not meaningfully different when compared with the overall sample. The relationship between priming and willingness was no longer significant (P=0.2) within this smaller subgroup.

Perceptions of the Relative Benefits of Sacubitril/Valsartan

Similar to willingness to take sacubitril/valsartan, the reported relative benefit of the drug compared with an ACE or ARB declined with rising prices (Table 2). On a 10-point Likert scale, the mean perceived benefit of sacubitril/valsartan over an ACE or ARB across all price conditions was 5.3 (SD, 2.3). At the $10 price conditions, individuals reported a relative benefit of

Table 1. Participant Demographic and Health Characteristics

Characteristic	Overall, n=1013	$10, cost priming, n=170	$50, cost priming, n=167	$100, cost priming, n=170	$10, no cost priming, n=167	$50, no cost priming, n=169	$100, no cost priming, n=170	*P* value
Age, y								0.9613*
18–29	14 (1.4)	5 (2.9)	4 (2.4)	2 (1.2)	0	2 (1.2)	1 (0.6)	
30–44	45 (4.4)	7 (4.1)	7 (4.2)	8 (4.7)	9 (5.4)	5 (3.0)	9 (5.3)	
45–59	195 (19.3)	35 (20.6)	29 (17.4)	38 (22.4)	30 (18.0)	31 (18.3)	32 (18.8)	
60+	759 (74.9)	123 (72.4)	127 (76.1)	122 (71.8)	128 (76.7)	131 (77.5)	128 (75.3)	
Sex								0.8879
Women	368 (36.3)	65 (38.2)	62 (37.1)	60 (35.3)	61 (36.5)	55 (32.5)	65 (38.2)	
Men	645 (63.7)	105 (61.8)	105 (62.9)	110 (64.7)	106 (63.5)	114 (67.5)	105 (61.8)	
Race and ethnicity								0.9984†
White, non-Hispanic	835 (82.4)	140 (82.4)	137 (82.0)	142 (83.5)	138 (82.6)	134 (79.3)	144 (84.7)	
Black, non-Hispanic	69 (6.8)	14 (8.2)	12 (7.2)	11 (6.5)	10 (6.0)	12 (7.1)	10 (5.9)	
Other¶, non-Hispanic	28 (2.8)	4 (2.4)	6 (3.6)	3 (1.8)	6 (3.6)	6 (3.6)	3 (1.8)	
Hispanic/Latino(a)	60 (5.9)	9 (5.3)	9 (5.4)	10 (5.9)	11 (6.6)	12 (7.1)	9 (5.3)	
2+ races, non-Hispanic	21 (2.1)	3 (1.8)	3 (1.8)	4 (2.4)	2 (1.2)	5 (3.0)	4 (2.4)	
Education								0.9770
High school graduate or less	326 (32.2)	50 (29.4)	52 (31.1)	57 (33.5)	52 (31.1)	54 (32.0)	61 (35.9)	
Some college (associates, trade school)	355 (35.0)	58 (34.1)	59 (35.3)	62 (36.5)	60 (35.9)	58 (34.3)	58 (34.1)	
Bachelor's degree	332 (32.8)	62 (36.5)	56 (33.5)	51 (30.0)	55 (32.9)	57 (33.7)	51 (30.0)	
Income								0.5576
<$25 000	152 (15.0)	29 (17.1)	22 (13.2)	27 (15.9)	21 (12.6)	23 (13.6)	30 (17.7)	
$25 000–$50 000	234 (23.1)	27 (15.9)	35 (21.0)	39 (22.9)	46 (27.5)	44 (26.0)	43 (25.3)	
$50 000–$75 000	202 (19.9)	31 (18.2)	32 (19.2)	40 (23.5)	31 (18.6)	37 (21.9)	31 (18.2)	
$75 000–$125 000	225 (22.2)	40 (23.5)	40 (24.0)	38 (22.4)	34 (20.4)	36 (21.3)	37 (21.8)	
>$125 000	200 (19.7)	43 (25.3)	38 (22.8)	26 (15.3)	35 (21.0)	29 (17.2)	29 (17.1)	
Self-reported health status								0.5935
Excellent	15 (1.5)	5 (2.9)	2 (1.2)	1 (0.6)	2 (1.2)	2 (1.2)	3 (1.8)	
Very good	181 (17.9)	33 (19.4)	38 (22.8)	21 (12.4)	32 (19.2)	23 (13.6)	34 (20.0)	
Good	447 (44.1)	69 (40.6)	73 (40.6)	86 (50.6)	72 (43.1)	78 (46.2)	69 (40.6)	
Fair	280 (27.6)	48 (28.2)	45 (27.0)	48 (28.2)	42 (25.2)	50 (29.6)	47 (27.7)	
Poor	88 (8.7)	15 (8.8)	9 (5.4)	13 (7.7)	19 (11.4)	16 (9.5)	16 (9.4)	
No answer	2 (0.2)	0	0	1 (0.6)	0	0	1 (0.6)	
Self-reported number of medications								0.9569
Median (IQR)‡	6 (4–8)	5 (4–8)	5 (4–9)	6 (4–8)	5 (4–8)	6 (4–8)	6 (4–9)	
Medical maximizer/minimizer in situations where it is not clear, do you tend to lean toward taking action or do you lean toward waiting and seeing if action is needed (scale 1–6)								
Mean (SD)§	3.4 (1.5)	3.3 (1.6)	3.6 (1.5)	3.5 (1.5)	3.5 (1.5)	3.3 (1.5)	3.3 (1.5)	0.3376
CFPB Financial Wellbeing Scale								
Mean (SD)‖	57.0 (15.1)	56.4 (17.1)	57.3 (15.0)	56.8 (14.1)	57.5 (14.6)	57.6 (13.7)	56.2 (15.8)	0.7817

CFPB indicates Consumer Financial Protection Bureau, and IQR, interquartile range.
*Ages 18 to 29 years and 30 to 44 years were combined because of sparse cell counts.
†Other and 2+ races were combined because of sparse cell counts.
‡There were 6 missing responses (n=1007).
§There were 12 missing responses (n=1001).
‖ There were 15 missing responses (n=998).
¶ "Other" category comprises of Asian, American Indian or Alaska Native, and Native Hawaiian/Pacific Islander.

Table 2. Patient Attitudes and Knowledge About Sacubitril/Valsartan by Out-of-Pocket Cost and Cost Priming

Question	Overall, n=1013	Out-of-pocket cost				Cost priming		
		$10, n=337	$50, n=336	$100, n=340	*P* value	Cost priming, n=506	No cost priming, n=507	*P* value
If you find out that your insurance covers the newer ARNI medicine and you would need to pay $__ per month for it, would you take it if your doctor recommended it?					<0.0001			0.0359
Yes, n (%)	603 (59.5)	286 (84.9)	206 (61.3)	111 (32.7)		319 (62.9)	284 (56.1)	
No, n (%)	403 (39.8)	51 (15.1)	126 (37.5)	226 (66.5)		183 (36.1)	220 (43.5)	
No answer, n (%)	7 (0.7)	0	4 (1.2)	3 (0.9)		5 (1.0)	2 (0.4)	
On a scale of 1–10, with 1 being no better and 10 being a lot better, how much better do you think the ARNI medicine is for patients with heart failure compared with an ACEI/ARB?*					<0.0001			0.4711
Mean (SD)	5.3 (2.3)	5.7 (2.2)	5.3 (2.3)	4.8 (2.3)		5.3 (2.3)	5.2 (2.3)	
If 100 people were to take the ARNI medication for 2 y, how many more people would be alive than if the same 100 people took an ACEI/ARB?					0.2382			0.7791
0–2, n (%)	61 (6.0)	17 (5.0)	22 (6.6)	22 (6.5)		30 (5.9)	31 (6.1)	
3, correct answer, n (%)	312 (30.8)	107 (31.8)	114 (33.9)	91 (26.8)		163 (32.2)	149 (29.5)	
4–100, n (%)	571 (56.4)	196 (58.2)	177 (52.7)	198 (58.2)		282 (55.6)	289 (57.1)	
No answer, n (%)	69 (6.8)	17 (5.0)	23 (6.9)	29 (8.5)		32 (6.3)	37 (7.3)	

ACEI indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; and ARNI, angiotensin receptor-neprilysin inhibitor.
*There were 9 missing responses (n=1004).

sacubitril/valsartan of 5.7 (SD, 2.2). This decreased to 5.3 (SD, 2.3) at the $50 price condition and further dropped to 4.8 (SD, 2.3) at the $100 price condition (*P*<0.0001 for trend). Perception of benefit did not vary across the cost-priming groups (5.3 versus 5.2, *P*=0.5; Table 2).

In multivariable ordinal logistic regression (Table 4), those exposed to the $10 price condition had higher odds of a greater perception of benefit compared with those exposed to the $100 price condition (OR, 2.2 [95% CI, 1.7–3.0]). Those exposed to the $50 price condition also had higher odds of having a greater perception of benefit than those exposed to the $100 price condition (OR, 1.5 [95% CI, 1.1–2.0]). Other significant predictors of greater perception of benefit included being a woman (OR, 1.5 [95% CI, 1.2–2.0]), making >$125 000 compared with <$25 000 (OR, 2.0 [95% CI, 1.2–3.3]), and being a medical maximizer (OR, 1.3 [95% CI, 1.2–1.4]).

DISCUSSION

Patients' OOP costs are a significant concern in the context of contemporary heart failure therapy,[24,25] but few studies have examined the extent to which patients' decisions are cost sensitive over the range of typical OOP costs. Our results suggest individuals' decisions about medications with a known mortality benefit are highly sensitive to cost and that a cost-priming intervention may impact willingness to take medications.

Most directly, our findings highlight the need to consider OOP costs when prescribing medications for HFrEF and other cardiac diseases. Much of the emphasis on shared decision making has been in the context of decisions where there are competing medical benefits or risks or where there are marginal benefits. Sacubitril/valsartan, however, has clear medical benefits and a similar safety profile to its alternatives. The tradeoff involved in deciding to switch to this medication primarily relates to cost. Although integrating price into clinical decisions rarely occurs today, price is an important consideration for initiating medication discussions that should be on the table during clinical encounters, and available evidence suggests that patients agree.[8,26]

Our findings also lend some support to concerns that cost may be playing a role in what many consider

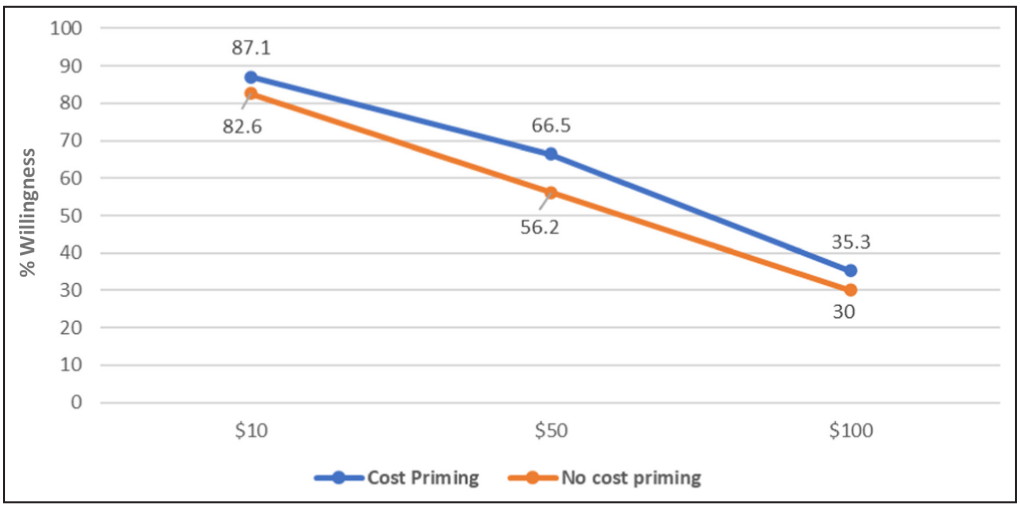

Figure 2. Willingness to take sacubitril/valsartan by monthly out-of-pocket cost and cost priming.

to be suboptimal uptake and adherence for sacubitril/valsartan.[27,28] Despite a guideline recommendation for sacubitril/valsartan as first-line therapy for HFrEF, most patients are not prescribed this medication and, of those who are prescribed it, only 59% continue taking it after 6 months.[27] Cost concerns are becoming increasingly salient in HFrEF more generally in the context of the recent influx of medications with demonstrated benefits for this population.[3,4,29–31] Though this study only examined sacubitril/valsartan, cost sensitivity is broadly relevant in selecting medications for patients with HFrEF and made more complicated by the fact the benefits associated with medications vary substantially in magnitude and type.[32]

It is also important to recognize potential financial toxicity. Financial toxicity has been framed as the adverse impact of treatment-related OOP costs and has been shown to impact nearly 1 in 3 patients with cardiovascular disease.[33] Patients with heart failure who report financial toxicity are not only less likely to adhere to prescribed medications but are also likely to have worse overall health.[34] Integrating medication cost discussions into shared decision-making may present an opportunity to mitigate financial toxicity and help patients make decisions that cohere with their preferences and personal financial constraints and goals.[26]

We also examined the impact of a novel cost-priming strategy in this study to learn how contextualizing OOP cost information can impact choices for sacubitril/valsartan. We hypothesized that individuals exposed to cost priming would be less likely to take the medication, but participants who were cost primed were more willing to take sacubitril/valsartan overall. Importantly, our data do not answer whether cost priming is desirable, and the primary reason to

Table 3. Multivariable Logistic Regression Model of Willingness to Take Sacubitril/Valsartan (n=978)

Effect	OR	95% CI
Cost		
$10 vs $100	14.347	9.441–21.803
$50 vs $100	3.594	2.530–5.106
Cost primed vs nonprimed	1.439	1.059–1.954
Age	1.006	0.993–1.020
Sex		
Women vs men	1.047	0.755–1.452
Race		
Black, non-Hispanic vs White, non-Hispanic	0.617	0.334–1.140
Other* vs White, non-Hispanic	0.639	0.390–1.047
Income		
$25 000–$50 000 vs <$25 000	1.448	0.878–2.387
$50 000–$75 000 vs <$25 000	2.098	1.236–3.561
$75 000–$125 000 vs <$25 000	2.485	1.433–4.306
≥$125 000 vs <$25 000	4.312	2.303–8.073
CFPB Financial Wellbeing Scale	1.013	1.001–1.026
Education		
High school graduate or lower vs bachelor's degree or higher	0.948	0.611–1.471
Some college vs bachelor's degree or higher	0.906	0.609–1.349
Self-rated health		
Good vs excellent/very good	0.840	0.538–1.313
Fair vs excellent/very good	0.735	0.448–1.204
Poor vs excellent/very good	0.761	0.389–1.489
Medical maximizer vs medical minimizer	1.327	1.198–1.470

CFPB indicates Consumer Financial Protection Bureau; and OR, odds ratio.

*"Other" category comprises of Asian, American Indian or Alaska Native, and Native Hawaiian/Pacific Islander.

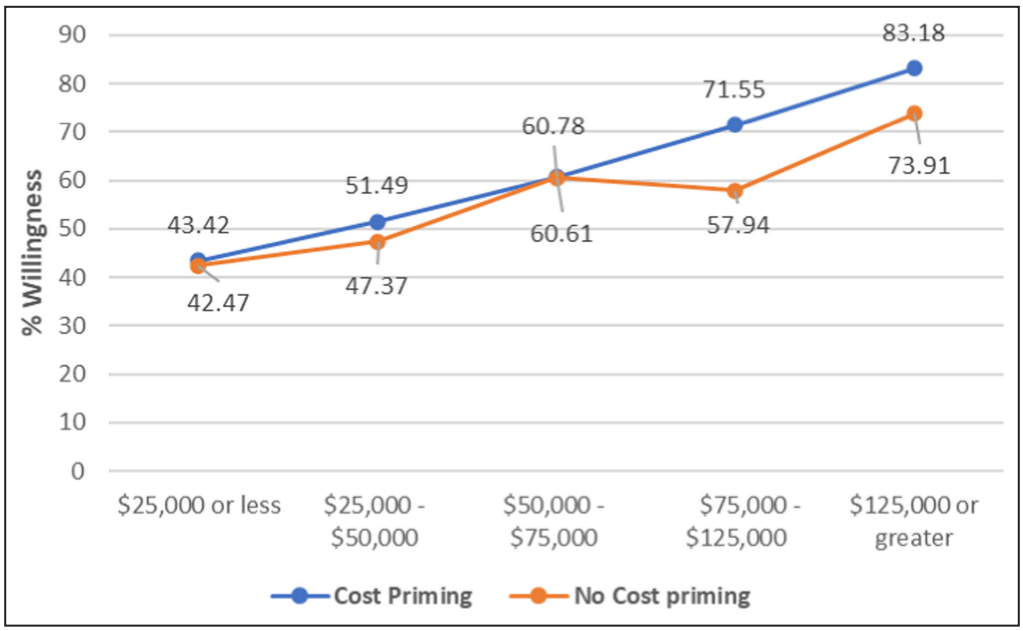

Figure 3. **Willingness to take sacubitril/valsartan by income and cost priming (n=1013).**

ask patients to consider their own financial situation before learning about a medication and its cost is not to promote uptake but rather to help patients contextualize information about the drug. As efforts to improve price transparency in health care increase, OOP costs will become more readily available. Our results suggest that how prices are contextualized and how conversations are structured could influence patients' decisions.

Although factors such as cost priming may impact patient willingness to take medications, our study only explored one strategy for structuring discussions. Priming and contextualizing interventions can take many forms, and further studies are needed to understand the implications of various strategies for integrating OOP cost information into clinical encounter, because the impact of these interventions can be unpredictable. Two recent clinical trials demonstrated modest impacts of eliminating OOP costs of medications for patients following acute coronary syndrome.[35,36] Robust prospective studies are needed to understand the extent to which different cost communication strategies do or do not impact decision making, adherence, and other outcomes for patients who have HFrEF.

Our study also highlights the fact that effectively integrating cost into medical decisions is not simple. Most participants did not correctly interpret the numeric benefits presented to them, and participants overall had a lukewarm view of the 3% absolute mortality benefit conferred by sacubitril/valsartan over an ACE or ARB. Across all price points, participants perceived sacubitril/valsartan to be marginally better than an ACE or ARB. This stands in stark contrast to the view among cardiologists that this drug is a "game changer" deserving of a guideline-recommendation.[37] The mismatch between perceptions of clinicians and patients, which is compounded by frequent incomplete understanding among patients, underscores the challenge of integrating costs into shared decision-making conversations. The ideal strategy to accurately communicate the value proposition of sacubitril/valsartan to patients remains unclear and raises important ethical questions. In addition, accurate out-of-pocket cost information is often unavailable during the clinical encounter. Although this information is likely to become more readily available via electronic medical record systems, its absence makes discussions about cost particularly challenging at present.

This study has several limitations. First, this experiment represented a hypothetical scenario. Participants were not making real-time decisions about initiation of sacubitril/valsartan, and we solicited stated preferences rather than observing revealed preferences. Second, our participants self-identified as having heart disease and did not necessarily have a diagnosis of HFrEF specifically. In this respect, these respondents may not represent views of patients with advanced heart failure. However, they reported an appreciable level of medication burden and were well-distributed in terms of self-reported health status. They were also demographically similar to the HFrEF population in many respects, though our respondent sample had a relatively higher proportion of college-educated individuals and a relatively lower proportion of Black respondents. In addition, the role of sacubitril/valsartan in advanced disease is not as well established,[38] and

Table 4. Multivariable Logistic Regression Model of Increased Perception of Benefit of Sacubitril/Valsartan (n=977)

Effect	OR	95% CI
Cost		
$10 vs $100	2.230	1.655–3.006
$50 vs $100	1.508	1.124–2.023
Cost primed vs nonprimed	0.952	0.748–1.210
Age	0.998	0.988–1.009
Sex		
Women vs men	1.504	1.160–1.951
Race and ethnicity		
Black, non-Hispanic vs White, non-Hispanic	1.528	0.933–2.503
Other* vs White, non-Hispanic	1.485	0.998–2.208
Income		
$25 000–$50 000 vs <$25 000	1.502	0.999–2.258
$50 000–$75 000 vs <$25 000	1.530	0.996–2.351
$75 000–$125 000 vs <$25 000	1.266	0.814–1.967
≥$125 000 vs <$25 000	1.996	1.224–3.253
CFPB Financial Wellbeing Scale	0.996	0.987–1.006
Education		
High school graduate or lower vs bachelor's degree or higher	1.158	0.816–1.643
Some college vs bachelor's degree or higher	0.820	0.602–1.119
Self-rated Health		
Good vs excellent/very good	0.967	0.691–1.353
Fair vs excellent/very good	0.947	0.647–1.385
Poor vs excellent/very good	1.008	0.599–1.697
Medical maximizer vs medical minimizer	1.320	1.218–1.432

CFPB indicates Consumer Financial Protection Bureau; and OR, odds ratio.

*"Other" category comprises of Asian, American Indian or Alaska Native, and Native Hawaiian/Pacific Islander.

prior work with a smaller sample of patients with diagnosed HFrEF demonstrated similar perspectives.[8] Importantly, further studies are needed to assess how OOP costs affect real world medication decisions for patients with HFrEF. Finally, respondents of an online survey panel may differ in other ways from actual patients, but the use of the Knowledge Panel mitigates these concerns to some extent. It uses rigorous address-based sampling and provides access to individuals without internet access; our study also had a high response rate.

CONCLUSIONS

In individuals with self-reported heart disease, increasing OOP costs of sacubitril/valsartan resulted in a substantial decrease in individuals' willingness to take the medication, and priming them to consider their own financial situation before learning about the drug increased their willingness to take it. Participants' perceived benefit of sacubitril/valsartan was relatively low overall and declined as price increased. Our findings highlight that decisions on initiation of sacubitril/valsartan and other higher-cost medications for HFrEF are preference sensitive and support efforts to integrate cost into patient-centered decision making.

ARTICLE INFORMATION

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Affiliations

Division of Cardiology, Department of Medicine (B.R.R., C.D.S., A.A.M., N.W.D.) and Department of Family and Preventive Medicine (M.A.M.), Emory University School of Medicine, Atlanta, GA; Department of Medicine, University of Colorado School of Medicine, Aurora, CO (L.A.A., D.D.M., L.D.S.); Palliative and Advanced Illness Research (PAIR) Center and Department of Medicine, Pennsylvania Perelman School of Medicine, Philadelphia, PA (S.D.H.); Department of Biostatistics (Y.-A. K.) and Department of Epidemiology (N.W.D.), Emory University Rollins School of Public Health, Atlanta, GA; Medical College of Georgia at Augusta University, Augusta, GA (M.C.T.); and Duke University Fuqua School of Business, Durham, NC (P.U.).

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Supplemental Material

Table S1
Figures S1–S2

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SUPPLEMENTAL MATERIAL

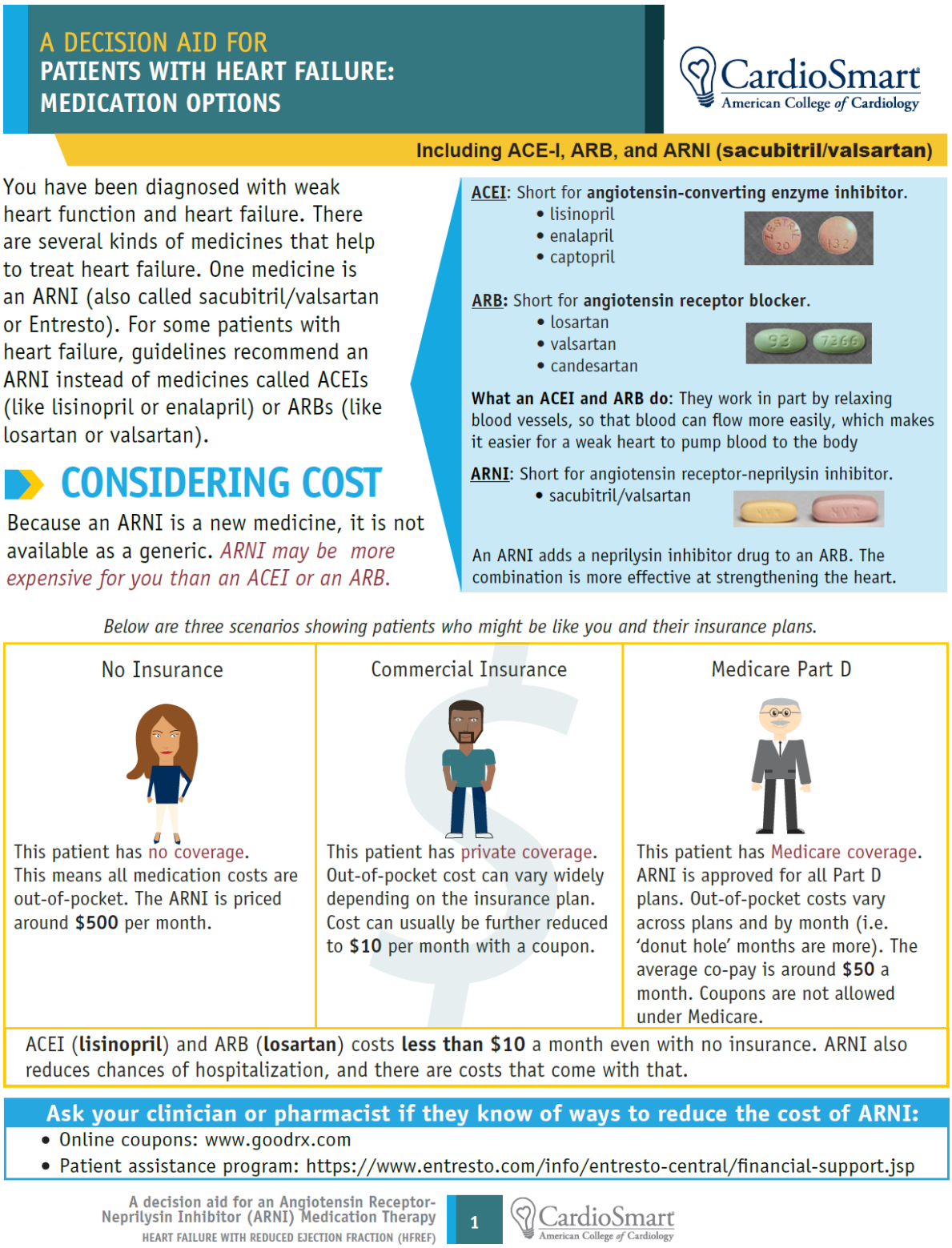
Table S1. Consumer Financial Protection Bureau Financial Wellbeing Scale by Cost Priming Scenario.

How well does this statement describe you or your situation?	Cost priming (n=507)	No cost priming (n=506)	Overall (n=1013)	p-value
Because of my money situation, I feel like I will never have the things I want in life				0.2379
Completely	46 (9.07)	33 (6.52)	79 (7.80)	
Very Well	38 (7.50)	39 (7.71)	77 (7.60)	
Somewhat	166 (32.74)	170 (33.60)	336 (33.17)	
Very Little	126 (24.85)	147 (29.05)	273 (26.95)	
Not at all	128 (25.25	110 (21.74)	238 (23.49)	
No Answer	3 (0.59)	7 (1.38)	10 (0.99)	
I am just getting by financially				0.3867
Completely	54 (10.65)	37 (7.31)	91 (8.98)	
Very Well	71 (14.00)	87 (17.19)	158 (15.60)	
Somewhat	166 (32.74)	168 (33.20)	334 (32.97)	
Very Little	97 (19.13)	95 (18.77)	192 (18.95)	
Not at all	115 (22.68)	113 (22.33)	228 (22.51)	
No Answer	4 (0.79)	6 (1.19)	10 (0.99)	
I am concerned that the money I have or will save won't last				0.2138
Completely	68 (13.41)	62 (12.25)	130 (12.83)	
Very Well	62 (12.23)	78 (15.42)	140 (13.82)	
Somewhat	172 (33.93)	162 (32.02)	334 (32.97)	
Very Little	114 (22.49)	119 (23.52)	233 (23.00)	
Not at all	91 (17.95)	81 (16.01)	172 (16.98)	
No answer	0	4 (0.79)	4 (0.39)	
I have money left over at the end of the month.				0.4931
Always	123 (24.26)	136 (26.88)	259 (25.57)	
Often	119 (23.47)	96 (18.97)	215 (21.22)	
Sometimes	140 (27.61)	148 (29.25)	288 (28.43)	
Rarely	78 (15.38)	81 (16.01)	159 (15.70)	
Never	46 (9.07)	45 (8.89)	91 (8.98)	
No Answer	1 (0.20)	0	1 (0.10)	
My finances control my life				0.8275
Always	55 (10.85)	49 (9.68)	104 (10.27)	
Often	75 (14.79)	85 (16.80)	160 (15.79)	
Sometimes	166 (32.74)	165 (32.61)	331 (32.68)	

Rarely	145 (28.60)	138 (27.27)	283 (27.94)	
Never	65 (12.82)	66 (13.04)	131 (12.93)	
No Answer	1 (0.20)	3 (0.59)	4 (0.39)	
Financial Well-being Score				
Mean (SD)*	56.8 (15.4)	57.1 (14.7)	57.1 (15.1)	0.7817

***There were 15 missing responses (n=998)**

Figure S1. Decision Aid For sacubitril/valsartan.

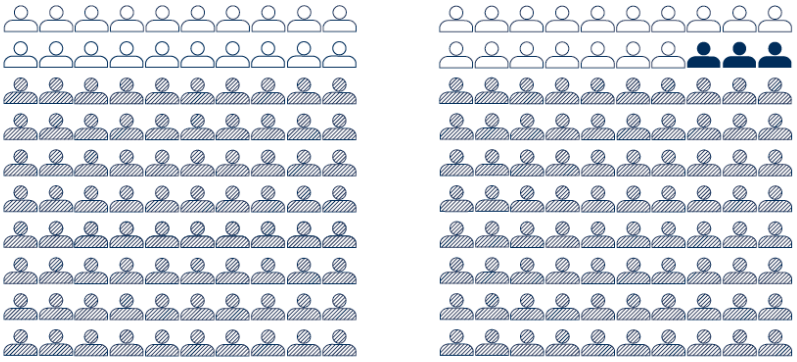


BENEFITS OF ARNI

The picture below shows the survival benefit of ARNI compared to ACEI/ARB (based on a large research study):

After two years on an ACEI, 80 of 100 patients were still living and 20 died.

After two years on an ARNI, 83 of 100 patients were still living and 17 died.



- Died within 2 years
- Lived
- Saved on an ARNI

Compared to other medicines, this is actually a pretty big benefit.

Patients *also* had a similar 3% decrease in hospitalization. In other words, 3 (out of 100) fewer patients went to the hospital because of heart failure while on an ARNI.

BURDENS AND RISKS

ACEI or ARB		*ARNI*
A pill taken by mouth, usually **once** or **twice** a day.	**How it is taken**	A pill taken by mouth, **twice** a day
Cough can occur with an **ACEI**	**Risks and Side Effects**	**Dizziness** is more common with an **ARNI** than with an ACEI

All 3 medication types can cause:

- low blood pressure
- high blood potassium
- kidney problems
- allergic reactions

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Figure S2. Sensitivity Analysis of Willingness to take sacubitril/valsartan among participants who understood its benefit (n=312).