Discussing Out-of-Pocket Costs With Patients: Shared Decision Making for Sacubitril-Valsartan in Heart Failure

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Background—"Financial toxicity" is a concern for patients, but little is known about how patients consider out-of-pocket cost in decisions. Sacubitril-valsartan provides a contemporary scenario to understand financial toxicity. It is guideline recommended for heart failure with reduced ejection fraction, yet out-of-pocket costs can be considerable.

Methods and Results—Structured interviews were conducted with 49 patients with heart failure with reduced ejection fraction at heart failure clinics and inpatient services. Patient opinions of the drug and its value were solicited after description of benefits using graphical displays. Descriptive quantitative analysis of closed-ended responses was conducted, and qualitative descriptive analysis of text data was performed. Of participants, 92% (45/49) said that they would definitely or probably switch to sacubitril-valsartan if their physician recommended it and out-of-pocket cost was $5 more per month than their current medication. Only 43% (21/49) would do so if out-of-pocket cost was $100 more per month (*P*<0.001). At least 40% across all income categories would be unlikely to take sacubitril-valsartan at $100 more per month. Participants exhibited heterogeneous approaches to cost in decision making and varied on their use and interpretation of probabilistic information. Few (20%) participants stated physicians had initiated a conversation about cost in the past year.

Conclusions—Out-of-pocket cost variation reflective of contemporary cost sharing substantially influenced stated willingness to take sacubitril-valsartan, a guideline-recommended therapy with mortality benefit. These findings suggest a need for cost transparency to promote shared decision making. They also demonstrate the complexity of cost discussion and need to study how to incorporate out-of-pocket cost into clinical decisions. (*J Am Heart Assoc*. 2019;8:e010635. DOI: 10.1161/JAHA.118. 010635)

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In the movement toward patient-centered care and shared decision making, out-of-pocket costs are often ignored. Cost communication appears infrequent between physicians and patients. In 2 recent studies, <20% of patients reported discussing costs with physicians.[1,2] Patient decision aids also rarely incorporate cost. "Financial toxicity," however, is a real concern.[3] Higher out-of-pocket medical costs can lead to forgone care and adverse health outcomes.[4–6] They may also negatively impact medication adherence.[7] Especially for patients with low income, modest costs may affect choices outside of health care. Without addressing financial implications in clinical encounters, it is difficult to align medical decisions with patients' global values, preferences, and financial resources.

Out-of-pocket cost has become particularly important for patients with heart failure with reduced ejection fraction (HFrEF) with the introduction of sacubitril-valsartan. With no new drugs approved in the United States for this condition between 2004 and 2015, standard of care was composed of several low-cost generic medications. This "game-changing"

Clinical Perspective

What Is New?

- This study suggests that out-of-pocket cost is a potentially meaningful driver of decisions for patients with heart failure with reduced ejection fraction that may make decisions about guideline-recommended therapies preference sensitive.

What Are the Clinical Implications?

- It is important for clinicians to develop approaches to providing and discussing out-of-pocket costs in the setting of heart failure treatment.

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drug was demonstrated to reduce the combined end point of cardiovascular mortality and heart failure hospitalization by 4.7% (absolute reduction) over 27 months compared with enalapril.[8] Replacing inexpensive angiotensin-converting enzyme inhibitors (ACE-Is) or angiotensin receptor blockers with sacubitril-valsartan received a class I recommendation in recent heart failure guidelines.[9] However, the retail price of sacubitril-valsartan is ≈$4500 a year; out-of-pocket costs vary widely and can exceed $100 a month for many insured patients.[10] This may be a significant concern, particularly for patients with fixed or low income and those who are ineligible for drug assistance. Moreover, patients with HFrEF have, on average, >4 other diseases and take nearly 10 medications.[11] Although its benefits are significant, cost may make taking sacubitril-valsartan a preference-sensitive decision.

There are numerous barriers to incorporating costs in medication decisions: clinicians' time is limited; out-of-pocket costs are often difficult for clinicians and patients to access; and cost discussions can be uncomfortable and sensitive. In addition, little is known about how patients weigh costs against medical benefits and how to present these tradeoffs to patients. Sacubitril-valsartan provides an excellent case for studying cost communication. The objective of this study was to explore how medication costs might impact patients' decisions about sacubitril-valsartan and explore patient preferences on cost discussions with clinicians.

Methods

Study Design

This was a cross-sectional interview study that mixed qualitative and quantitative elements. Structured interviews were conducted with patients with HFrEF. All interviews were conducted in person, and participants received a $25 gift card. Written informed consent was obtained. The study was approved by the Emory University Institutional Review Board.

Data supporting the findings of this study are available from the corresponding author on reasonable request for purposes of reproduction of results.

Setting and Participants

Potential participants were screened and recruited from heart failure clinics and inpatient services using convenience sampling. Eligibility criteria included: age ≥18 years, left ventricular ejection fraction ≤40%, eligibility for sacubitril-valsartan (on the basis of guidelines), and ability to provide informed consent.[9] Patients with a history of heart transplant, inotrope dependence, mechanical circulatory support, or dialysis dependence were excluded. Non–English-speaking patients were excluded because of the interactive nature of the interviews and English-speaking interviewers.

A provision for stratified sampling to ensure racial diversity was developed but was not necessary. Participants were approached during a clinic visit or hospitalization or by telephone in advance of their visit.

The planned sample size was 50 participants. Consistent with the hypothesis-generating goals of this study, this sample was chosen to provide reasonable point estimates of prevalence of views about an unexplored topic.

Interview Guide

A structured, interactive interview guide was developed by the investigators. It was cognitively and functionally pretested to ensure adequate communication about the drug, clarity of graphical displays, and comprehension of questions.

The interview guide (Data S1) contained open- and closed-ended questions in 4 major domains: health status; demographic and financial information; views of sacubitril-valsartan and its costs; and experiences and views of cost discussion in clinical encounters. Health status was assessed using the Euroquol 5D-3L and by asking participants to rate their current state of health and anticipated health in the next 5 years.[12] Demographic and financial data included race, sex, age, education level, employment status, financial status, annual income, monthly medication costs, and a single-question health literacy screen.[13]

Views of the drug and its costs were solicited after description of its benefits using 3 sets of graphical displays on the basis of PARADIGM-HF (Prospective Comparison of ARNI With ACEI to Determine Impact on Global Mortality and Morbidity in Heart Failure) data.[14,15] These displays demonstrated the impact of sacubitril-valsartan on all-cause mortality, hospitalization, and combined hospitalization or cardiovascular mortality (Figure) over a 2-year period (described as 2 years rather than 27 months for simplicity). Participants were informed that adverse effects were similar
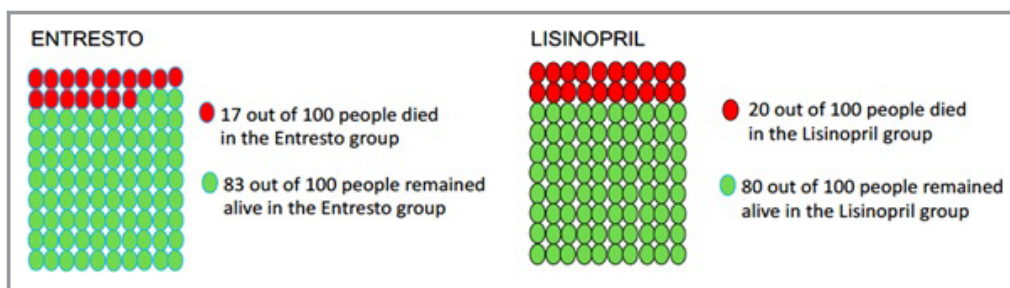
Figure. Example display of all-cause mortality benefit of sacubitril-valsartan (Entresto).

between sacubitril-valsartan and ACE-Is/angiotensin receptor blockers. A standardized script with this information preceded each display. Interviewers briefly confirmed understanding of information and allowed participants to ask questions before asking further questions. Participants were then asked about their willingness to change (without reference to cost or physician recommendation) to sacubitril-valsartan using a 5-point Likert scale. They were then asked their willingness to change to the drug if recommended by their physician under 2 different cost scenarios: $5 more per month than their current medication; and $100 more per month than their current medication. Open-ended probing questions were asked to reveal factors driving decision making and assess the impact of higher costs on participants' lives. Individuals willing to switch under the $5 but not the $100 scenario were asked the maximum they would be willing to pay.

Additional domains included views and experiences on cost discussion with clinicians (analyzed separately). Interviews generally lasted 20 to 30 minutes and were conducted by trained interviewers (G.S. and S.S.). Interviewers clarified that the study and research team members did not receive payment from any drug company related to this study.

Data Management

All interviews were audiorecorded and transcribed verbatim. Transcripts were redacted by a second study team member (A.M.). Questions with predefined response categories and demographic data were entered into Microsoft Excel. Data entry was verified during transcription review.

Quantitative Analysis

Quantitative data were analyzed using SAS 9.4 (SAS Institute, Cary, NC). Descriptive statistics were tabulated for patient characteristics and questions about costs. Fisher exact tests were performed to examine potential associations between cost responses and patient characteristics. McNemar tests were performed to examine whether the proportion of participants willing to take sacubitril-valsartan varied under different cost scenarios. Statistical significance was defined as $P<0.05$.

Qualitative Analysis

Transcripts of open-ended responses were analyzed using MAXQDA. The primary analytic aim was qualitative description (ie, providing rich description of reasons for particular responses and understanding the range of views and reasons for views in key domains).[16] A template analytic method was used.[17] In addition to specific codes in key domains, interviews were characterized on the general approach (decider type) the participant took on sacubitril-valsartan decisions.

A preliminary codebook was developed a priori by the research team on the basis of the guide and responses in pretesting. This codebook was expanded and refined inductively as themes emerged during transcript review (constant comparison). The codebook was considered finalized after review of the codebook and coding of a subset of interviews. All interviews were coded using the final codebook. Interviews were primarily coded by a single coder (G.S.) and double coded by at least one additional reviewer (N.D., C.S., or S.S.). Discrepancies were resolved by consensus. To enhance transparency, all instances of codes of primary analytic interest were reviewed by the research team to ensure they represented a coherent theme.

Results

Participant Characteristics

Fifty-four patients were approached; 50 were interviewed (response rate, 93%). One interview was excluded because of incomplete audiorecording. Median age was 57 years (interquartile range, 44–70 years), 43% were women, and 41% were black (Table 1). Education level and income were relatively evenly distributed, and 31% felt "somewhat" or less confident filling out medical forms. Approximately half (49%) had trouble affording discretionary items or paying bills, and median monthly medication cost was $75 (interquartile range, $25–$150). Only 4% of participants did not have insurance, 43% had Medicare, 35% had private insurance, and 18% had Medicaid. Most (80%) were not taking sacubitril-valsartan at the time of enrollment. Only 10 (20%) participants said a provider had asked them about medication costs in the past year.

Table 1. Patient Characteristics (n=49)

Characteristics	Values
Demographic information	
Age, y	57 (44–70)
Sex	
Female	21 (43)
Male	28 (57)
Race/ethnicity	
Black	20 (41)
White	28 (57)
Hispanic	1 (2)
Education	
High school graduate or less	19 (39)
Some college	12 (25)
College graduate or more	18 (37)
Income, US $	
<25 000	18 (37)
25 000–100 000	16 (33)
100 000–200 000	7 (14)
>200 000	3 (6)
Refused	5 (10)
Health literacy: how confident are you filling out medical forms by yourself?	
Extremely confident	22 (45)
Quite a bit confident	12 (25)
Somewhat confident	9 (18)
A little confident	3 (6)
Not at all confident	3 (6)
Currently taking sacubitril-valsartan	10 (20)
Interview site	
A	24 (49)
B	25 (51)
Health status	
In general, would you say your health is:	
Excellent	1 (2)
Very good	3 (6)
Good	20 (41)
Fair	20 (41)
Poor	5 (10)
Mobility	
I have no problems in walking about	21 (43)
I have some problems in walking about	27 (55)
I am confined to bed	1 (2)
Self-care	

Table 1. Continued

Characteristics	Values
I have no problems with self-care	43 (88)
I have some problems washing or dressing myself	5 (10)
I am unable to wash or dress myself	1 (2)
Usual activities	
I have no problems with performing my usual activities	21 (43)
I have some problems with performing my usual activities	23 (47)
I am unable to perform my usual activities	5 (10)
Pain/discomfort	
I have no pain or discomfort	22 (45)
I have moderate pain or discomfort	21 (43)
I have extreme pain or discomfort	6 (12)
Anxiety/depression	
I am not anxious or depressed	26 (53)
I am moderately anxious or depressed	21 (43)
I am extremely anxious or depressed	2 (4)
EuroqUol Visual Analog Scale (range, 0–100)	70 (50–80)
Euroqdol 5D-3L Index score	0.80 (0.71–0.84)
What do you think your health would be like in the next 5 years if you continued your current treatment with heart failure?	
Excellent	7 (14)
Very good	11 (23)
Good	12 (25)
Fair	10 (20)
Poor	9 (18)
Financial status	
Financial situation	
After paying the bills, you still have enough money for special things that you want	25 (51)
You have enough money to pay the bills, but little spare money to buy extra or special things	14 (29)
You have money to pay the bills, but only because you have to cut back on things	5 (10)
You are having difficulty paying the bills, no matter what you do	3 (6)
Refused	2 (4)
Monthly medication costs, US $	75 (25–150)

Data are given as median (interquartile range) or number (percentage).

The median EQ-5D-3L index score of the study population was 0.80 (interquartile range, 0.71–0.84), consistent with relatively mild disease.[18] However, more than half reported at least some issues with mobility, at least moderate pain, and

current health as fair or poor (Table 1). Most participants (61%) believed their health would be good, very good, or excellent in the next 5 years if they continued current heart failure treatment.

Likelihood of Taking Sacubitril-Valsartan Under Various Cost Scenarios

The first scenario asked participants about willingness to switch to sacubitril-valsartan after scripted description of benefits and graphical displays reflecting PARADIGM-HF results (Figure). *No cost language was included, and it was not stated whether their physician recommended sacubitril-valsartan.* Thirty-five participants (71%) said they would likely switch to sacubitril-valsartan (Table 2).

In the second scenario, participants were asked whether they would likely switch to sacubitril-valsartan *if their physician recommended it and incremental out-of-pocket cost*

Table 2. Sacubitril-Valsartan Cost Scenarios

Scenarios	Values
Assuming you are taking a drug like lisinopril, after hearing about this medicine, would you want to change to sacubitril-valsartan (Entresto)?	
1: Definitely yes	18 (37)
2: Probably yes	17 (35)
3: Do not know	7 (14)
4: Probably no	6 (12)
5: Definitely no	1 (2)
On the basis of your current health expenses and income, if sacubitril-valsartan cost $5 a month more than your current medication, would you want to change your current medication if your *physician recommended* it?	
1: Definitely yes	25 (51)
2: Probably yes	20 (41)
3: Do not know	0
4: Probably no	2 (4)
5: Definitely no	2 (4)
I want to imagine now that sacubitril-valsartan cost $100 a month more than your current medication. If your *physician recommended* it, would you want to change to it?	
1: Definitely yes	12 (25)
2: Probably yes	9 (18)
3: Do not know	3 (6)
4: Probably no	15 (31)
5: Definitely no	10 (20)
If answered do not know, probably no, or definitely no to $100 more: What is the most you would decide to pay for the new medicine? (n=25, 3 did not answer)	$15 ($10–$25)

Data are given as number (percentage) or median (interquartile range).

was $5. Forty-five participants (92%) said they would be likely to switch in this scenario, more than in the first scenario (*P*=0.0039).

In the third scenario, participants were asked whether they would likely switch *if their physician recommended it and incremental out-of-pocket cost was $100*. Twenty-one participants (43%) said they would likely switch. This is reduced compared with the $5 scenario (*P*<0.001). Among those unlikely to take the medication at $100, the median amount they were willing to pay was $15 (interquartile range, $10–$25).

Reasons for Not Switching to Sacubitril-Valsartan

Individuals unlikely to take sacubitril-valsartan (in any scenario) were asked for their reasons. Although cost played a large role, other prevalent reasons emerged that did not center around cost but substantially affected patients' perceptions of the drug's value. Some of these reasons focused on relative benefits (or lack thereof) of sacubitril-valsartan or its alternatives. For example, some participants viewed the drug as only marginally better than previous heart failure therapies (ACE-I and angiotensin receptor blocker) and regarded the benefits as insufficient to justify a switch. As one participant said, "Well I mean there really isn't much difference, variation between the 2 is a minor amount" (participant 122 734). These statements were more prevalent in the $100 scenario. Other participants did not want to change because they felt their current treatment was working well. For example, "[I'm] afraid to rock the boat or make any changes when I'm doing well" (participant 92 650).

Other non–cost-based reasons were focused more on risk. Potential adverse effects were mentioned by some as a reason for not wanting to take sacubitril-valsartan. This was driven by personal experience with adverse effects in the past or experiences of someone they knew with adverse effects to sacubitril-valsartan or other medications. These concerns were typically not specific to sacubitril-valsartan and were raised despite interviewers' descriptions of the drug as having similar adverse effects to ACE-I and angiotensin receptor blocker. Fewer participants were generally distrustful of new medications. They were concerned about unanticipated adverse effects or risks that might arise once a drug was available on a wider scale. They seemed to favor drugs that had been on the market for longer.

Relationship Between Willingness to Change ($100 Scenario) and Participant Characteristics

Responses to the $100 scenario were stratified by health literacy, income, education, race, and 5-year expected health (Table 3) to provide preliminary insights into potential relationships or drivers of responses. Although there were numeric differences in willingness to switch at $100 within all

Table 3. Willingness to Change ($100 Scenario) and Participant Characteristics

Characteristics	Yes	No/Do Not Know	P Value
Health literacy (confidence filling out forms)			0.36
Extremely confident	13 (59)	9 (41)	
Quite a bit confident	3 (25)	9 (75)	
Somewhat confident	3 (33)	6 (67)	
A little confident	1 (33)	2 (67)	
Not at all confident	1 (33)	2 (67)	
Income, US $			0.40
<25 000	6 (33)	12 (67)	
25 000–100 000	8 (50)	8 (50)	
>100 000	6 (60)	4 (40)	
Refused	1 (20)	4 (80)	
Education			0.27
High school or less	8 (42)	11 (58)	
Some college	3 (25)	9 (75)	
College or more	10 (56)	8 (44)	
Race/ethnicity			0.24
Black	11 (55)	9 (45)	
White	10 (36)	18 (64)	
Hispanic	0 (0)	1 (100)	
5-y Health expectation			0.21
Excellent	3 (43)	4 (57)	
Very good	7 (64)	4 (36)	
Good	6 (50)	6 (50)	
Fair	4 (40)	6 (60)	
Poor	1 (11)	8 (89)	

Data are given as number (percentage).

categories, these differences were not statistically significant. Across all groups, a substantial number of participants said they would be unlikely to switch to sacubitril-valsartan at the higher price. For example, 4 of 10 participants (40%) with income >$100 000 a year stated that they would be unlikely to take it at $100 more per month.

Participants with worse 5-year health expectations were numerically less likely to want to switch to sacubitril-valsartan at $100 than those with better 5-year health expectations. Only 1 of the 9 participants (11%) who said they expected their health to be poor was likely to switch.

Approaches to Decision About Sacubitril-Valsartan

Participants reflected a range of decision-making approaches in response to open-ended probes about their willingness to take the drug under different scenarios. More important, most participants exhibited multiple approaches to decision making.

The most commonly used approach was cost-benefit analysis. These decisions were driven by weighing stated benefits of the drug against its costs (Table 4). This is distinctive from "straight cost analysis," in which participants focused simply on whether they could afford the drug without specific mention of potential benefits. Most of the participants (78%) exhibited some form of cost analysis.

Seven participants were specifically averse to cost considerations, stating their health was so important that they would not want cost to affect their decision about whether to take a recommended medication. These individuals sometimes expressed concerns about cost, acknowledged that affording the medication could involve significant sacrifice, and recognized that cost could be prohibitive. However, they stated a strong desire to avoid cost as a basis for a decision.

Other approaches, often concurrent with cost concerns, involved considerations other than probabilistic information. Some participants viewed their physician's recommendation as most important. Sometimes they considered cost-benefit tradeoffs and other factors as well, but their physician's suggestion was the driving factor rather than their assessment of benefits as presented. For others, a priority was maintaining the status quo. These patients did not want to change medication for fear that things could get worse. Finally, some individuals stated that personal experience or others' experience with sacubitril-valsartan drove their assessment.

Discussion

Using the example of sacubitril-valsartan in HFrEF, this study provides insights into the potential role of cost in shared decision making for beneficial but expensive medications. Cost discussions are infrequent in clinical encounters, there may be multiple barriers to integration of costs into decisions, and little is known about how patients view tradeoffs between out-of-pocket cost and medical benefit. However, because out-of-pocket costs matter to patients, cost is highly relevant for clinical decision making.

The most striking finding is the decrease in willingness (43% versus 92%) to take sacubitril-valsartan in the high ($100) versus low ($5) cost scenario. Many cardiologists would argue the decision about sacubitril-valsartan in eligible patients is not preference sensitive, because it is guideline recommended, has demonstrated superiority over ACE-I, and is well tolerated. However, the change in willingness observed in this study demonstrates that cost may make this decision preference sensitive and appropriate for a shared decision-making approach. Although much of the shared decision-making

Table 4. Approaches to Decision About Sacubitril-Valsartan

Decider Type	Example Quotations
Cost-benefit analysis	P: Cause $100 is just too much for medicine ain't it? It's not that much difference in the charts, 2 or 3 people out of 100.
Straight cost analysis	I: Can you tell me more about how you decided on this answer? Because you told me you were not doing that well on lisinopril. P: It's strictly because of finances, and if it's that much more I can't do anything about it.
	I: Definitely no. Can you tell me more about how you decided about this answer? P: Just off a budget. Cause right now what I am paying is high now with my copays so to do an increase definitely wouldn't work, being on disability.
Health above all	P: If it's going to strengthen my heart and save my life it wouldn't matter.
	P: I mean if it was $1000 a month or something just outrageous, I probably would have to really think about it because, you know, in a year that's really going to add up, but at the end of the day if it's something that can save your life-there's no price.
Physician's recommendation is what matters	P: I'm going to say I don't know because I want to discuss it further with my physician. I: Sure. P: I don't believe that mass results necessarily relate to any one given... I put more faith in the opinion of my own physician.
Status quo based	P: If it's working you know like I said, "If it ain't broke then don't fix it."

I indicates interviewer; P, participant.

literature has focused on decisions that are medical "toss-ups," this finding demonstrates that factors other than medical risks and benefits can make shared decision making important.

It is also notable that these data suggest cost may be relevant across a range of copayments and patients. The current distribution of copayments across payers for sacubitril-valsartan is unknown; however, $100 is well within the range of current copayments, especially for patients ineligible for pharmaceutical assistance programs (eg, those covered by Medicare part D). Moreover, the median price most people stated they were willing to pay per month (who were not willing to pay $100) was $15. Concerns about cost are likely to be prevalent for this medication, and they do not appear to be limited to situations in which individuals have very high copayments.

Similarly, cost sensitivity was not isolated to low-income patients. A substantial number of people in every stratum of our population stated they would be unlikely to take sacubitril-valsartan under the $100 cost scenario. Despite the fact that there was a numeric increase in willingness to take the drug as income increased, 4 of 10 individuals with annual income > $100 000 were unlikely to take it in the $100 scenario. Price thus has special salience in populations with financial barriers but may be relevant across all patient populations. More important, more work needs to be done to explore patients' conceptions of value for medication.

In addition to highlighting the importance of cost integration, the study provides insights into the complexities and hazards of cost discussions. First, patients approached cost-related decisions in heterogeneous ways. Some explicitly engaged in cost-benefit tradeoffs, whereas others rejected cost as a basis for decisions altogether. Still others made "straight-cost" decisions about what they can afford. Cost will thus play different roles in decisions for different patients. Second, patients illustrated different uses of probabilistic information. Many patients did not explicitly use numeric data in their assessments about the drug, and a "physician's recommendation" was often highly influential. Some patients clearly saw this as a life or death situation on the basis of the data presented and did not appreciate the incremental benefit of sacubitril-valsartan. Others dismissed the drug's important benefits as minimal or meaningless. Both interpretations are problematic. Certainly, trivializing a nearly 3% absolute risk reduction in mortality is worrisome when this reduction is as significant as (and is additive to) many other guideline-recommended HFrEF therapies.

Together, these findings reinforce that implementing shared decision making can be difficult and that the presentation of evidence in encounters is likely to matter substantially. Numeric framing effects (eg, presentation of absolute or relative risks and survival versus mortality data), anchoring effects related to understanding of present prognosis, and whether it is mentioned that this drug is guideline recommended will likely impact patients' decisions. Careful attention to these issues, and avoidance of frames that inappropriately accentuate or minimize risks or benefits, is

essential. However, entirely neutral presentations in the context of a guideline-recommended therapy with a demonstrated mortality benefit may also not be ideal.[19]

One surprising finding was that participants with a less favorable view of their future were numerically less frequently willing to switch to sacubitril-valsartan. This finding was not statistically significant, but we had predicted that the reverse relationship would exist, that individuals with a worse outlook would be more eager to change. This phenomenon may represent a form of status quo bias that warrants further study and illustrates the psychological and emotional complexity of many decisions in serious chronic illness.

Limitations

Several limitations should be acknowledged. First, this was an exploratory study with a small sample; these findings are hypothesis generating. Second, participants were from a single health system in a geographically small area, although they were diverse in age, sex, race/ethnicity, education level, and income. Third, the scenarios were hypothetical. This was necessary to examine decisions under varying scenarios, but these decisions may not reflect decisions in practice. Related, there may be an order effect of the $5 and $100 cost scenarios, although this is unlikely to explain the dramatic shift we observed. Future studies should be done within actual physician-patient encounters and can elucidate, for example, whether cost has played a role in driving slower than expected uptake of sacubitril-valsartan.[20] Fourth, some participants were already taking the drug and may have different views. Fifth, the effect of framing is unavoidable when administering interview questions and presenting probabilistic data. The interview guide was designed to be balanced (eg, presenting absolute risk rather than relative risks), but understanding of absolute risk may be limited, and ideal framing of this information is not established. Finally, selection bias is possible with small sample size and convenience sampling, although the diversity of the population and a high response rate (93%) lessen this concern.

Conclusion

Out-of-pocket cost may play an important, complex role in decisions about sacubitril-valsartan and other medications with significant benefits. In this respect, the decision about whether to switch a patient with HFrEF to sacubitril-valsartan can become preference sensitive despite a guideline recommendation and robust medical evidence.[9] This study adds to growing literature suggesting the importance of integrating cost into shared decision making despite the fact that such conversations are rare. These findings also clarify that approaches to decisions about sacubitril-valsartan and cost-

benefit tradeoffs vary among patients. Successful integration of out-of-pocket cost into shared decision making requires significant further research.

Disclosures

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Data S1.

Interview Guide

Introductory script
Thank you for participating in our research study. We want to learn more about how patients think about choices that they make with their doctors about different medicines. In particular, we want to know more about how patients think about costs associated with different medicines.

Just to remind you, your responses are confidential. They will not be shared with anyone outside of the research team. They will not be given, for example, to your doctor. However, you can certainly ask your doctor if you have any questions about any of the medicines we ask you about in this survey.

Participation is entirely voluntary. You may choose to not answer any question that makes you feel uncomfortable. Filling out the survey will not affect your medical care in any way. And if you decide not to fill out the survey, that will not affect your medical care either.

You should know that the questions we ask about cost are not designed to be used to set drug prices. **We have no connection with drug companies or insurance companies**. Our goal is to understand how patients think about prices of medicines and how patients want their doctors to help them make decisions when cost is a consideration.

Health Status Assessment

In general, would you say your health is:

Excellent	❑
Very good	❑
Good	❑
Fair	❑
Poor	❑

By marking one box in each group below, please indicate which statements best describe your own health today.

Mobility

I have no problems in walking about ❑

I have some problems in walking about ❑

I am confined to bed ❑

Self-Care

I have no problems with self-care ❑

I have some problems washing or dressing myself ❑

I am unable to wash or dress myself ❑

Usual Activities *(e.g. work, study, housework, family or leisure activities)*

I have no problems with performing my usual activities ❑

I have some problems with performing my usual activities ❑

I am unable to perform my usual activities ❑

Pain / Discomfort

I have no pain or discomfort ❑

I have moderate pain or discomfort ❑

I have extreme pain or discomfort ❑

Anxiety / Depression

I am not anxious or depressed ❑

I am moderately anxious or depressed ❑

I am extremely anxious or depressed ❑

To help you classify how healthy you feel, we have drawn a scale for you to report how good or bad your health is in general; 100 being full health for someone your age and 0 being as bad as dead.

To indicate how healthy you feel, please circle a point on the scale and write its corresponding numerical value in the space below.

Your own health in general_____ (Please write a number)

**Best Health for
Someone Your Age**

100
90
80
70
60
50
40
30
20
10
0

**Equivalent to
dead**

Recently a medication called Entresto has been approved for patients with congestive heart failure. Compared to a medication similar to Lisinopril, using Entresto led to more people being alive and more people avoiding having to be hospitalized for congestive heart failure over two years. The side effects are similar between these medicines. I want to show you some pictures that might help to understand what the major study showed about this medicine's benefits for patient with heart failure.

Each circle in these figures is a patient with congestive heart failure. Imagine that there are 100 people in each group, one group received Entresto and the other Lisinopril. Circles that are green in color are patients who were alive at the end of 2 years and circles that are red are patients who died within 2 years. So, this study showed that if 100 people took Entresto for two years, about 17 of 100 patients died after 2 years (meaning 83 of them would have survived). If the same 100 people had taken Lisinopril, about 20 of them died after 2 years (meaning 80 of them would have survived). So 3 fewer people out of 100 died when taking Entresto.

ENTRESTO
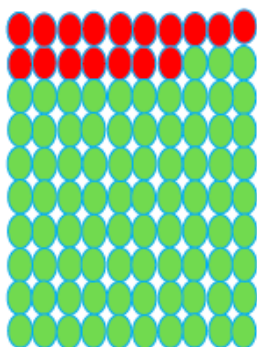
17 out of 100 people died
in the Entresto group

83 out of 100 people remained
alive in the Entresto group
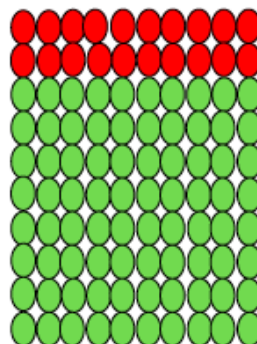
LISINOPRIL

20 out of 100 people died
in the Lisinopril group

80 out of 100 people remained
alive in the Lisinopril group

The Entresto medicine also helped some people to avoid having to be in the hospital. Each circle in the figure below is again a patient. Circles that are yellow are patients who were hospitalized because of congestive heart failure in 2 years and circles that are green are patients who were not hospitalized in 2 years. This same study showed that if 100 people took Entresto for two years, about 13 of them would be hospitalized for heart failure during that time (meaning 87 of them would not). If the same 100 people had Lisinopril, about 16 of them would be hospitalized (meaning 84 of them would not). So 3 fewer people out of 100 had to be hospitalized over 2 years when taking Entresto. The pictures below show a picture of the differences between these medicines.

ENTRESTO
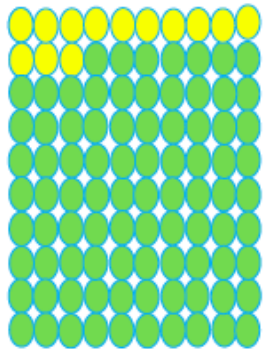
○ 13 out of 100 patients were hospitalized in the Entresto group

○ 87 out of 100 patients had no hospitalizations in the Entresto group
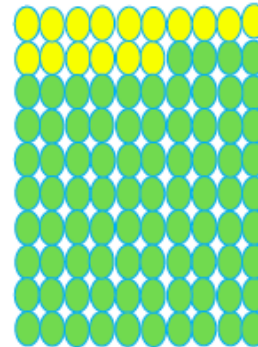
LISINOPRIL

○ 16 out of 100 patients hospitalized in the Lisinopril group

○ 84 out of 100 patients had no hospitalizations in the Lisinopril group

What I showed you before were pictures of how Entresto affected whether people lived or died over a 2 year period, and how it affected whether they stayed out of the hospital. Some patients did have both things happen to them (they were hospitalized and later died). The last picture I want to show you puts together the effects of Entresto on whether people survived and whether they got hospitalized.

Each circle here is again an individual patient. Any circles that are red or have a tinge of red are patients who died within 2 years. Any circles that are yellow or have a tinge of yellow are patients who were hospitalized due to congestive heart failure within 2 years. So circles that are part red and part yellow are patients who were both hospitalized and who died within 2 years. Circles that are green are patients who were never hospitalized for congestive heart failure and who survived at the end of 2 years.

ENTRESTO
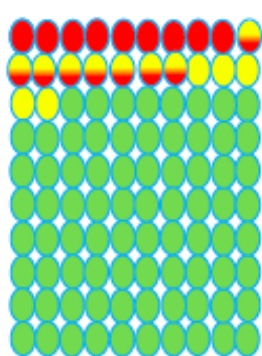
- 17 out of 100 people died in the Entresto group over 2 years
- 13 out of 100 people were hospitalized in the Entresto group over 2 years
- 8 out of 100 people were hospitalized and died in the Entresto group over 2 years
- 78 out of 100 people remained alive without hospitalizations in the Entresto group over 2 years

LISINOPRIL AND SIMILAR MEDICATIONS
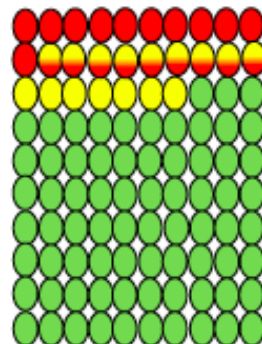
- 20 out of 100 people died in the Lisinopril group over 2 years
- 16 out of 100 people were hospitalized in the Lisinopril group over 2 years
- 9 out of 100 people were hospitalized and died in the Lisinopril group over 2 years
- 73 out of 100 people remained alive without hospitalizations in the Lisinopril group over 2 years

Tell me in your own words what the figure above shows.

BENEFIT THRESHOLD

1. Assuming you are taking a drug like Lisinopril, after hearing about this medicine, would you want to change to Entresto?

❏1	❏2	❏3	❏4	❏5
Definitely Yes	Probably Yes	Don't Know	Probably No	Definitely No

If patient says I don't know or Im not sure – ask tell me more about what you mean.

2. Tell me a little bit about how you came to this decision?

COST THRESHOLD

Now we want to ask your thoughts about how you would think about the cost of the new medicine in deciding about whether to take it. In answering the next few questions, we want you to keep in mind your current health expenses and available money.

3. Based on your current health expenses and income, if Entresto cost $5 a month more than your current medication, would you want to change your current medication if your doctor recommended it? I'll show you again the same picture of the number of people who might live longer taking Entresto compared to the Lisinopril and similar medications.

ENTRESTO
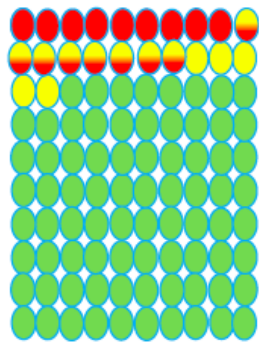
LISINOPRIL AND SIMILAR MEDICATIONS

17 out of 100 people died in the Entresto group over 2 years

13 out of 100 people were hospitalized in the Entresto group over 2 years

8 out of 100 people were hospitalized and died in the Entresto group over 2 years

78 out of 100 people remained alive without hospitalizations in the Entresto group over 2 years

Cost: $10 per month
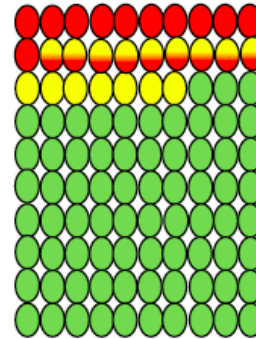
20 out of 100 people died in the Lisinopril group over 2 years

16 out of 100 people were hospitalized in the Lisinopril group over 2 years

9 out of 100 people were hospitalized and died in the Lisinopril group over 2 years

73 out of 100 people remained alive without hospitalizations in the Lisinopril group over 2 years

Cost: $5 per month

[If signs that they do not understand] Check if they understand the figure with a question like In which group did more patients survive. In which group did more patients stay out of the hospital?

❑₁
Definitely
Yes

❑₂
Probably
Yes

❑₃
Don't Know

❑₄
Probably
No

❑₅
Definitely
No

Can you tell me about how you decided on this answer?

What do you think your reaction would be to finding out that Entresto cost $5 per month more?

4. Now I want you to think about a different situation but still based on your current health expenses and income. I want to imagine now that Entresto cost 100 dollars a month more than your current medication. If your doctor recommended it, would you want to change to it? Again, the same picture shows the differences in how people do when they take Entresto versus when they take lisinopril.

ENTRESTO
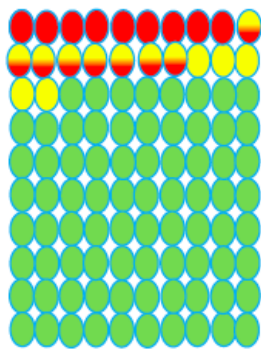
● 17 out of 100 people died in the Entresto group over 2 years

○ 13 out of 100 people were hospitalized in the Entresto group over 2 years

◑ 8 out of 100 people were hospitalized and died in the Entresto group over 2 years

● 78 out of 100 people remained alive without hospitalizations in the Entresto group over 2 years

Cost: $105 per month

LISINOPRIL AND SIMILAR MEDICATIONS

● 20 out of 100 people died in the Lisinopril group over 2 years

○ 16 out of 100 people were hospitalized in the Lisinopril group over 2 years

◑ 9 out of 100 people were hospitalized and died in the Lisinopril group over 2 years

● 73 out of 100 people remained alive without hospitalizations in the Lisinopril group over 2 years

Cost: $5 per month

❑₁   ❑₂   ❑₃   ❑₄   ❑₅
Definitely   Probably   Don't Know   Probably   Definitely
Yes   Yes   No   No

Can you tell me how you decided on this answer?

If your doctor were to tell you that the new drug, Entresto, would cost you $100 more a month, what do you think your reaction would be?

How would paying $100 per month for this medicine affect you? (Follow-up as appropriate with probes related to ability to afford other medications, etc.)

If you got to the pharmacy and found out that the drug would cost you $100 per month, what do you think you would do? If say yes to 100 USD: Is there any amount you wouldn't pay?

If say no to 100 USD then ask Q5:

5. Below is the same picture of the number of people who might live longer taking Entresto compared to the the standard medicine. We are interested in knowing what you feel like you would be willing to pay for the new medicine.
The current medicine costs $5 every month. What is the most you would **decide** to pay for the new medicine?
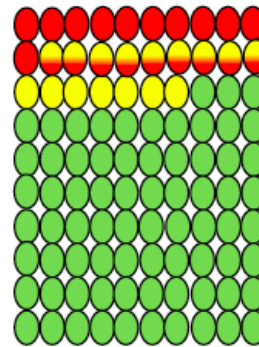
ENTRESTO
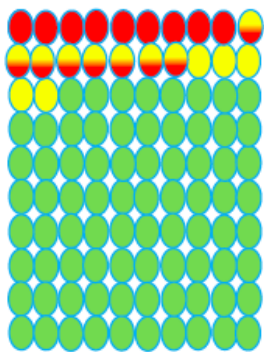
🔴 17 out of 100 people died in the Entresto group over 2 years

🟡 13 out of 100 people were hospitalized in the Entresto group over 2 years

🔴🟡 8 out of 100 people were hospitalized and died in the Entresto group over 2 years

🟢 78 out of 100 people remained alive without hospitalizations in the Entresto group over 2 years

Cost: $_ per month

LISINOPRIL AND SIMILAR MEDICATIONS
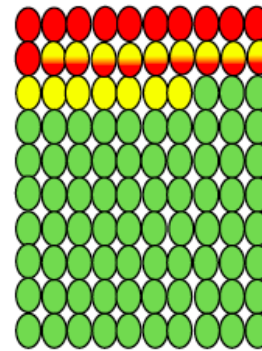
🔴 20 out of 100 people died in the Lisinopril group over 2 years

🟡 16 out of 100 people were hospitalized in the Lisinopril group over 2 years

🔴🟡 9 out of 100 people were hospitalized and died in the Lisinopril group over 2 years

🟢 73 out of 100 people remained alive without hospitalizations in the Lisinopril group over 2 years

Cost: $5 per month

6. We mentioned that Entresto helped some people to stay alive longer. If a drug did not potentially help you live longer but might help to reduce the chance of being in the hospital would that change your decision about wanting to take it?
   Probe: would it change what you would be willing to pay for it?

7. We are conducting this study to understand how patients want physicians to communicate with them about medication costs. How would you like your physicians to talk with you about cost of your medications?

Probes: Who should introduce, how should they introduce it, what information would you want to know before starting a medication, how should this be presented?

8. Have you ever had issues with affording medications that your doctor has prescribed?
   Probes: Can you tell me more about these situations affected you/your health?

9. How did you handle this situation? (paid for it/skipped meds/told your doctor).

10. How comfortable are you with approaching financial discussions with your doctor?

11. In the past, how helpful have you found your doctors to be in addressing concerns about costs regarding medications?
    Probes: Tell me more about these situations (who initiated the conversation? what did the physician do? Switch to other meds, discuss benefits, arrange for samples?)

12. How frequently do your doctors initiate conversations about healthcare costs you are facing?
    Probes: How long do these discussions typically last/how do they go?

13. Currently, which parts of your healthcare are you most concerned about in terms of costs (medications, hospitalizations, physician visit)?

Please answer the following questions to help us understand your background: (Some questions below may be repeated)

1. What is your age?

2. What is your gender?

3. Please indicate your highest level of education:
   ❑ Some high school

❑ High school graduate (Diploma or GED)
❑ Some college, Associate's degree, and/or trade school
❑ College graduate
❑ Post graduate degree

4. Are you currently employed?
❑ Full time employed

❑ Part time employed

❑ Unemployed

❑ Retired

❑ Other

5. For approximately how many years have you been living with congestive heart failure?

6. What do you think your health would be like in the next 5 years if you continued your current treatment with heart failure?

❑ 1	❑ 2	❑ 3	❑ 4	❑ 5
Excellent	Very good	Good	Fair	Poor

7. How many times have you had to be in hospital during the last one year?

8. How would you describe your household's financial situation right now? Would you say:
❑ After paying the bills, you still have enough money for special things that you want

❑ You have enough money to pay the bills, but little spare money to buy extra or special things

❑ You have money to pay the bills, but only because you have cut back on things

❑ You are having difficulty paying the bills, no matter what you do

9. How much do you pay for your medications on a monthly basis?

10. In the past 12 months, how often have you been unable to take medications as prescribed due to their cost?

$\square_1$ $\square_2$ $\square_3$ $\square_4$ $\square_5$

Never **Rarely**   **Occasionally**   **Frequently**   **Very frequently**

11. In the past 12 months, how often did a doctor of a nurse ask you about your medication costs?

$\square_1$ $\square_2$ $\square_3$ $\square_4$ $\square_5$

Never **Rarely**   **Occasionally**   **Frequently**   **Very frequently**

How helpful were they when you talked to them about problems paying for your medication?

$\square_1$ $\square_2$ $\square_3$ $\square_4$ $\square_5$

Never **Rarely**   **Occasionally**   **Frequently**   **Very frequently**

12. In the past 12 months, how often did you tell a nurse or a doctor **in advance** that you will have to take less medication due to cost?

$\square_1$ $\square_2$ $\square_3$ $\square_4$ $\square_5$

Never **Rarely**   **Occasionally**   **Frequently**   **Very frequently**

13. In the past 12 months, how often did you tell a nurse or doctor **after** taking lesser medication than prescribed due to cost?

$\square_1$ $\square_2$ $\square_3$ $\square_4$ $\square_5$

Never **Rarely**   **Occasionally**   **Frequently**   **Very frequently**

14. How good are you at doing the following things:
    a) How good are you at working with fractions?

$\square_1$ $\square_2$ $\square_3$ $\square_4$ $\square_5$ $\square_6$

Not at all   **Extremely**

good   **good**

b) How good are you at working with percentages?

❑1   ❑2   ❑3   ❑4   ❑5   ❑6

Not at all   **Extremely**

good   **good**

15. When people tell you the chance of something happening, do you prefer that they use **words** ("it rarely happens") or **numbers** ("there's a 1% chance")?

❑1   ❑2   ❑3   ❑4   ❑5   ❑6

Always prefer   **Always prefer**

words   **numbers**

16. How often do you have difficulty in understanding your physician during discussions relating to medication costs, benefits and side-effects?

❑1   ❑2   ❑3   ❑4   ❑5

Never   Rarely   Occasionally   Frequently   Very frequently

17. How confident are you filling out medical forms by yourself?

❑ Extremely confident

❑ Quite a bit confident

❑ Somewhat confident

❑ A little confident

❑ Not at all confident

18. Please indicate your annual income

❑ <$25,000

❑ $25,000 - $50,000

❑ $50,000-$100,000

❑ $100,000 - $ 200,000

❑ >$200,000