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US physicians' decision-making during buprenorphine-naloxone treatment: Conjoint analyses of dose and office visit adjustments based on patient progress

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ABSTRACT

Background: Research on how US physicians individualize buprenorphine-naloxone treatment is limited. The current study uses conjoint analysis to examine the importance of current dose, visit frequency, clinical indicators, and payment type on office visit and dose adjustments during buprenorphine-naloxone treatment.
Methods: A national random sample of 776 US buprenorphine-prescribing physicians participated in a mailed survey between October 2015 and July 2018. The survey contained 16 patient vignettes describing: (1) current dose, (2) urine drug test (UDT) results and opioid blockade, (3) recent intravenous use, (4) visit attendance, (5) counseling adherence, (6) payment, and (7) visit schedule. Physicians rated how they would adjust office visits (0 = definitely decrease to 5 = no change to 10 = definitely increase) and the dose (0 = definitely decrease to 5 = no change to 10 = definitely increase). Descriptive statistics were calculated for the vignette responses. Conjoint analysis was used to estimate relative importance scores and part-worth utilities.
Results: Across the vignettes, the mean response for adjusting office visits was 7.43 (SD = 1.69), indicating a tendency to increase the frequency of visits. UDT results/opioid blockade, intravenous use, and current visit schedule had the greatest importance scores for office visit adjustments. The mean response for adjusting the dose was 5.48 (SD = 1.69), corresponding with a tendency toward not changing dose. Current dose, UDT results/opioid blockade, and intravenous use had the largest importance scores for dose adjustment.
Conclusions: Physicians individualized buprenorphine-naloxone treatment in response to hypothetical patient attributes by changing visit frequency and, to a lesser extent, modifying maintenance dose, in a manner generally consistent with current practice guidelines.

1. Introduction

The United States is currently experiencing elevated rates of opioid use disorder (OUD), a chronic and often relapsing illness, with recent estimates of prevalence ranging from 2.4 to 5 million people (Kolodny et al., 2015; Substance Abuse and Mental Health Services Administration, 2017a). The negative consequences of untreated OUD include increased mortality risk, infectious disease acquisition and transmission, and criminal justice involvement (Volkow et al., 2014). Buprenorphine-naloxone delivered in combination with medical management, and often with other psychosocial interventions, is effective (Fiellin et al., 2008) but under-utilized (Jones et al., 2015; Substance Abuse and Mental Health Services Administration, 2017b). Little is known about how providers implement this treatment, particularly how they respond to indicators of clinical progress, which has implications for treatment retention and OUD remission. The current study describes

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physicians' approaches to two key clinical decisions for modifying care during a buprenorphine-naloxone treatment episode: adjusting a patient's dose and changing the frequency of office visits with the prescribing physician.

Clinical practice guidelines encourage providers to respond to clinical indicators throughout the treatment process (American Society of Addiction Medicine, 2015; Substance Abuse and Mental Health Services Administration, 2018; World Health Organization, 2009). US guidelines recommend weekly office visits initially but are less specific about a timetable for reducing visit frequency, other than noting that visits can decrease for stable patients. Monthly visits are only recommended for very stable patients (American Society of Addiction Medicine, 2015; Substance Abuse and Mental Health Services Administration, 2018). International guidelines also specify that patients should be seen on at least a monthly basis (World Health Organization, 2009).

US and international guidelines recommend daily doses of buprenorphine-naloxone of 8–24 mg (in Suboxone® equivalents), but higher doses (up to 32 mg daily) may be appropriate if there is ongoing opioid use (American Society of Addiction Medicine, 2015; Substance Abuse and Mental Health Services Administration, 2018; World Health Organization, 2009). Ongoing opioid use is relatively common in randomized clinical trials (RCTs). For example, Fudula et al. (2003) reported about 33% of urine tests were opioid-positive at 52 weeks of treatment (dose range: 8–24 mg/daily). Continued opioid use may indicate insufficient withdrawal suppression and/or opioid blockade due to an insufficient dose. For some patients, opioid-positive urine drug tests may indicate that patients are not taking their medication optimally or their prescribed dosage. US guidelines recommend a maximum dose of 24 mg, although some data suggest doses up to 32 mg daily, with observed daily dosing (i.e., licensed opioid treatment programs [methadone clinics] in the US), are positively associated with treatment retention (Hser et al., 2014).

Previous physician surveys have not addressed how office visit frequency and dose may change during a treatment episode. Few surveys have reported how frequently physicians see patients, with the exception of Yang et al. (2013) who found only about one-third of physicians saw patients more frequently than once per month. Some surveys have described dosing practices. In an early study of waivered physicians, respondents reported the majority of their patients were receiving doses of ≤16 mg (Arfken et al., 2010). More recently, the majority in a small sample of prescribers in San Diego indicated their patients averaged ≤12 mg (MacDonald et al., 2016), while New York City prescribers reported a median maintenance dose of 16 mg (Kermack et al., 2017). Administrative claims data show average doses of 13–17 milligrams per day (Gordon et al., 2015; Lo-Ciganic et al., 2016; Manhapra et al., 2018; Shcherbakova et al., 2018). While these studies offer information about typical dosing practices, it remains unknown how physicians individualize patients' doses in response to clinical indicators. It is unknown whether physicians titrate the frequency of office visits in response to similar clinical indicators.

1.1. Conjoint analysis as a method to study decision-making during the treatment process

To study clinical decision-making during buprenorphine-naloxone treatment, the current study employed conjoint analysis, which extends upon the tradition of clinical case vignettes for understanding physician decision-making. Peabody et al. (2000) demonstrated that case vignettes more accurately measured physician behavior than chart abstraction.

Conjoint analysis utilizes an experimental model to construct case vignettes through an orthogonal design that determines the most efficient number of vignettes needed to study the relative impact of specific factors hypothesized to be relevant to decision-making (Luce and Tukey, 1964; Orme, 2010). The vignettes are presented in a survey. By presenting multiple pieces of information within each vignette, conjoint analysis is better able to approximate real-life decision-making than typical self-report survey measures (Ryan and Farrar, 2000; Sattler and Hensel-Borner, 2003).

Because real-life decision-making typically requires evaluation of multiple factors (Stevens and Jason, 2015), conjoint analysis is a powerful methodology for studying decision-making related to the management of buprenorphine-naloxone patients. For example, some patients may arrive at their office visit with signs and symptoms indicating the resumption of opioid use, while other patients may show continued progress toward OUD remission. Physicians must evaluate multiple sources of information, including physical signs of visible intravenous track marks, reported euphoria from continued opioid use, adherence to the treatment plan, and results from urine drug testing, in considering whether a patient would benefit from changes in dose and office visit frequency.

Building on our prior work (Knudsen et al., 2018), the current study uses conjoint analysis to estimate US physicians' decision-making regarding dose and visit adjustments in a novel set of vignettes. By examining the factors of dose and visit adjustments with the same set of vignettes, the present study assesses the contribution of clinical indicators to decision-making on these two key practice behaviors. This study also presents descriptive data regarding typical practices related to dose and office visits.

2. Methods

2.1. Sample and data collection

The conjoint analyses draw upon survey data collected from a sample of randomly selected physicians from all US states and the District of Columbia who prescribe buprenorphine-naloxone for treating OUD. A baseline cohort was randomly sampled from the May 2014 issue of the US Drug Enforcement Agency's Controlled Substances Act (CSA) Active Registrants database. To be eligible, physicians must be treating at least one OUD patient with buprenorphine. Baseline surveys were completed by 1174 physicians (33.0% response rate). Full details of the baseline recruitment have been published (Knudsen et al., 2018).

This cohort was invited to participate in a second survey approximately 12 months after the baseline survey. Survey procedures were identical to baseline and included a notification letter, an express-mailed study packet, a postcard reminder at two weeks, and a follow-up telephone reminder and second study packet to non-respondents after six weeks. Of the baseline participants, 69 physicians were ineligible for follow-up due to no longer prescribing buprenorphine (n = 9), retirement (n = 14), or the survey being undeliverable (n = 46). Between October 2015 and July 2018, 776 physicians participated, representing 70.2% of the baseline cohort who were eligible (n = 1105). Physicians provided written informed consent and were compensated US$100. This study was approved by the University of Kentucky's Medical Institutional Review Board (Protocol 13-0068-P6J), and all study procedures adhered to the Declaration of Helsinki.

2.2. Baseline measures of physician characteristics

Physician characteristics measured at baseline (Table 1) included demographic characteristics. An open-ended question about medical specialty was coded into a typology of three mutually exclusive groups: addiction specialties (e.g., addiction medicine, addiction psychiatry), general psychiatry, and all others, which largely consisted of family medicine and internal medicine. Waiver type was extracted from the May 2014 CSA database, which at the time of baseline recruitment, was either 30 or 100 patients. Finally, physicians indicated in which of six settings they delivered buprenorphine-naloxone treatment, choosing multiple settings if applicable.

Table 1
Characteristics of buprenorphine-naloxone prescribers at baseline (N = 776).

	Mean (SD) or % (N)
Age in years	55.6 (11.2)
Female	22.2% (171)
Race/ethnicity	
White	79.1% (602)
Asian	11.6% (88)
African American/Black	3.9% (30)
Hispanic	3.8% (29)
Multiracial/Other	1.6% (12)
Medical specialty	
Addiction (e.g., addiction psychiatry or addiction medicine)	23.6% (180)
Psychiatry	26.9% (205)
All other specialties	49.5% (377)
Waiver type as of May 2014	
Up to 30 patients	42.5% (330)
Up to 100 patients	57.5% (446)
Buprenorphine-naloxone practice setting	
Individual medical practice	50.3% (385)
Group medical practice	36.2% (277)
Veterans Administration medical center (VAMC)	4.8% (37)
Hospital (non-VAMC)	13.1% (100)
Opioid treatment program (OTP)	5.9% (45)
Substance use disorder program (non-OTP)	14.8% (113)

Notes. Due to rounding error, some percentages may sum to more than 100%. The questions about practice setting allowed physicians to indicate multiple settings.

2.3. Conjoint vignettes and primary outcome ratings

The conjoint vignettes consisted of seven attributes, with four attributes having three levels (i.e., pieces of information) and three attributes with two levels. Attributes and levels were based on clinical practice guidelines, qualitative interviews with 21 buprenorphine, and our team's clinical expertise, an approach similar to other conjoint studies (Bridges et al., 2011). Because a full factorial design would have required 648 vignettes (3*3*3*2*2*3*2 = 648), we used *IBM SPSS*'s suite of conjoint analysis commands to build the vignettes by entering each attribute and number of levels. The resulting orthogonal design indicated 16 vignettes were needed and specified the levels for each vignette.

Instructions were presented before the first vignette, indicating that all patients were receiving buprenorphine-naloxone, doses were in Suboxone® equivalents, and time in treatment was 3 months. We selected this treatment length because the first two months are typically a stabilization period before the maintenance stage (Gordon and Krumm, 2013). Table 2 presents a summary of the levels for each vignette. The precise wording of each level appears in Table 3; the full set of vignettes is available by request. After each vignette, two outcome ratings were presented. Physicians were asked, "How would you adjust the frequency of office visits (with you, the treating physician) for this patient?" Response options ranged from 0 to 10, where 0 represented "definitely decrease the frequency of visits," 5 represented "make no change," and 10 represented "definitely increase the frequency of visits." Then, physicians were asked, "How would you adjust the daily milligram dose for this patient?" Responses options ranged from 0 to 10, where 0 = definitely decrease, 5 = make no change, and 10 = definitely increase the dose.

2.4. Measures of typical practices regarding office visits and doses

Physicians were asked about the typical frequency of office visits after 2 months of treatment for stable patients (i.e., no ongoing substance use) and for unstable patients with ongoing drug use. For stable patients, responses were categorized as every two weeks or more frequently (= 1), monthly (= 2), or every two months or less frequently (= 3). For unstable patients, responses were categorized as weekly (= 1), every two weeks (= 2), monthly or less frequently (= 3), or patient would be discharged (= 4). Physicians reported the average daily dose and maximum dose in Suboxone® equivalents prescribed to stable patients. Responses were categorized based on the distribution for average dose (0 = ≤8 mg, 1 = 10–12 mg, 2 = 14–16 mg, and 3 = ≥16 mg) and maximum dose (0 = < 16 mg, 1 = 16 mg, 2 = 18–24 mg, and 3 = > 24 mg). These self-reported measures of typical practices were developed for this study and pre-tested during cognitive interviews conducted in advance of the baseline data collection.

2.5. Statistical analyses

Descriptive statistics were calculated for physician characteristics, dosing practices, and office visit schedules using *Stata 15.1*. To compare the characteristics of respondents to the follow-up survey and non-respondents, chi-square tests and t-t-tests were calculated with significance set at $p < .05$ (two-tailed test). After calculating descriptive statistics for both outcome ratings, *SPSS Conjoint* estimated the average relative importance of the seven attributes and the part-worth utilities for each level using complete case analysis. In our model, all levels were specified as categorical and the two outcome ratings represented scores, not ranks. Part-worth utilities represent regression coefficients indicating the direction of association, with larger part-worth utilities having greater influence on the outcome ratings (Orme, 2010). Importance scores are calculated using the part-worth utilities. To calculate each attribute's importance score, the range of its part-worth utilities (i.e., its smallest utility subtracted from its largest utility) is divided by the sum of the ranges for all attributes, and then multiplied by 100. Because average relative importance scores for the attributes always sum to 100, the magnitudes of the attributes can be compared.

3. Results

3.1. Physician characteristics

Professional and demographic characteristics of the sample of physicians who participated in this follow-up survey are presented in Table 1. There were no significant differences in these physician characteristics between respondents to the follow-up survey and non-respondents (results not shown).

3.2. Adjusting the frequency of office visits

Across the 16 vignettes, the overall mean for the office visit outcome rating was 7.42 (SD = 1.68; range = 0–10), indicating an overall tendency towards increasing the frequency of office visits in response to the vignettes. There was some variation across the 16 vignettes (Table 2). Means ranged from a low of 5.87 (SD 2.26 for patient vignette 9) to a high of 8.61 (SD = 2.41 for patient vignette 8).

Relative importance scores (RIS) for the office visit outcome appear in Fig. 1's dark gray bars. Attributes of greatest importance in relation to adjusting the frequency of office visits were UDT results/opioid blockade (RIS = 27.90), intravenous use (RIS = 24.75), and current visit schedule (RIS = 24.90). The remaining four attributes of current dose, attending the previous office visit, adhering to recommended counseling, and method of payment had importance scores that were relatively small, summing to only 22.5.

Part-worth utilities indicated the correlations between specific levels and the outcome rating (Table 3, Rating 1 column). For UDT/opioid blockade, the large positive part-worth utility for patients with the combination of usually opioid positive UDT and reports of euphoria indicated stronger preferences for increasing the frequency of office visits with such patients. Similarly, physicians were likely to increase the frequency of office visits when patients presented with currently

Table 2
Combinations of levels in 16 vignettes of patients receiving buprenorphine-naloxone treatment and descriptive statistics.

Patient Vignette	Current Daily Dose	Pattern of UDT, Blockade, & Benzodiazepine	Hx of IV Use & Current IV use	Previous Office Visit Attendance	Counseling Adherence	Method of Payment for Office Visits	Current Office Visit Frequency	**R1 Mean (SD)**	**R2 Mean (SD)**
1	24 mg	Usually O+ & euphoric from opioid use	No Hx of IV & no tracks	Attended	Adherent	Cash	Monthly	8.54 (2.17)	4.60 (2.64)
2	8 mg	Occasionally O+, no euphoria, recent B+	Hx of IV but no tracks	Attended	Adherent	Medicaid	Monthly	7.96 (2.20)	5.71 (2.30)
3	24 mg	Occasionally O+, no euphoria	Hx of IV but no tracks	Attended	Non-adherent	Private insurance	Bi-weekly	6.75 (2.46)	4.13 (1.93)
4	16 mg	Occasionally O+, no euphoria	Hx of IV but no tracks	Rescheduled at last minute	Adherent	Cash	Bi-weekly	6.11 (2.23)	5.19 (1.68)
5	8 mg	Occasionally O+, no euphoria, recent B+	Hx of IV & fresh tracks	Attended	Non-adherent	Cash	Bi-weekly	7.92 (2.53)	6.13 (2.86)
6	8 mg	Usually O+ & euphoric from opioid use	Hx of IV but no tracks	Rescheduled at last minute	Non-adherent	Medicaid	Monthly	8.57 (2.26)	6.99 (2.91)
7	16 mg	Occasionally O+, no euphoria, recent B+	No Hx of IV & no tracks	Rescheduled at last minute	Non-adherent	Private insurance	Monthly	8.17 (2.28)	4.79 (2.03)
8	24 mg	Occasionally O+, no euphoria	Hx of IV & fresh tracks	Rescheduled at last minute	Non-adherent	Medicaid	Monthly	8.61 (2.41)	4.15 (2.46)
9	8 mg	Occasionally O+, no euphoria	No Hx of IV & no tracks	Rescheduled at last minute	Adherent	Medicaid	Bi-weekly	5.87 (2.26)	5.83 (1.90)
10	24 mg	Occasionally O+, no euphoria, recent B+	No Hx of IV & no tracks	Rescheduled at last minute	Adherent	Medicaid	Bi-weekly	6.69 (2.42)	3.90 (2.03)
11	8 mg	Occasionally O+, no euphoria	No Hx of IV & no tracks	Rescheduled at last minute	Non-Adherent	Cash	Monthly	7.37 (2.32)	5.76 (2.15)
12	8 mg	Occasionally O+, no euphoria	No Hx of IV & no tracks	Attended	Non-adherent	Medicaid	Bi-weekly	6.16 (2.44)	5.73 (2.07)
13	8 mg	Occasionally O+, no euphoria	No Hx of IV & no tracks	Attended	Adherent	Private insurance	Monthly	6.33 (2.17)	5.79 (1.89)
14	16 mg	Usually O+ & euphoric from opioid use	No Hx of IV & no tracks	Attended	Non-adherent	Medicaid	Bi-weekly	7.57 (2.49)	6.05 (2.81)
15	8 mg	Usually O+ & euphoric from opioid use	Hx of IV & fresh tracks	Rescheduled at last minute	Adherent	Private insurance	Bi-weekly	7.97 (2.36)	7.38 (2.93)
16	16 mg	Occasionally O+, no euphoria	Hx of IV & fresh tracks	Attended	Non-adherent	Medicaid	Monthly	8.22 (2.28)	5.60 (2.45)

Notes. Each vignette consisted of seven bullet points with one level from each attribute. The two outcome ratings were presented after each vignette. Abbreviations: UDT = Urine drug test. Hx = History. IV = primary route has been intravenous. O+ = urine drug test usually positive for opioids. O- = urine drug test usually negative for opioids. B+ = urine drug test recently positive for illicit benzodiazepines. R1 = outcome rating 1 (office visits with the physician). R2 = outcome rating 2 (dose of buprenorphine-naloxone).

visible intravenous track marks. Physicians indicated a greater willingness to increase the frequency of office visits when the current visit schedule was on a monthly basis rather than biweekly basis.

3.3. Adjusting the dose of buprenorphine-naloxone medication

Physicians were also asked about how they would adjust the dose of medication that they prescribed to each patient (Table 2, Rating 2 column). The mean across the 16 vignettes was 5.48 (SD = 1.69), which corresponds to, on average, not making a change in dose. For 12 of the 16 vignettes, the median response was 5, which corresponded to no change. Patient vignette 10 had the lowest mean (3.90; SD = 2.03), a value in the direction of a dose reduction. Patient vignette 15 had the greatest mean (7.38; SD = 2.93), a value suggestive of a dose increase.

The three largest relative importance scores, as seen in Fig. 1's light gray bars, were for current dose (RIS = 50.12), UDT results/opioid blockade (RIS = 29.08), and recent intravenous use (RIS = 13.24). The attributes of office visit attendance, adherence to counseling, payment, and visit schedule had very low importance scores, summing to less than the importance score for recent intravenous use.

Part-worth utilities revealed the direction of associations between these attributes and dose adjustments (Table 3, Rating 2 column). Receiving an 8 mg daily dose was positively associated with a willingness to increase the dose. Conversely, being at a 24 mg daily dose was negatively associated with the outcome rating, indicating a preference for decreasing the patient's dose. The level of UDT results/opioid blockade that was indicative of inadequate opioid blockade (i.e., usually positive UDT results coupled with reported euphoria) had a positive part-worth utility, suggesting physicians were willing to increase the dose for such patients. In contrast, there was a negative association for patients with the combination of having only occasionally positive UDT results, no reports of opioid blockade, and a recent benzodiazepine-positive UDT. Finally, a history of injection drug use combined with current injection track marks resulted in a positive part-worth utility, indicating willingness to increase the dose.

3.4. Physicians' self-reported office visit and dosing practices

Physicians reported different strategies for office visits depending on whether the patient was stable or unstable after the first two months of treatment (Table 4). For stable patients with no ongoing substance use, nearly three-quarters of physicians reported a schedule of monthly office visits. When patients were unstable and had ongoing substance use, physicians reported seeing such patients more frequently. About 35.0% of physicians reported scheduling weekly visits, and 39.8% scheduled bi-weekly visits when patients showed signs of clinical instability. A small minority (6.3%) of the sample indicated they would no longer see such patients.

Regarding buprenorphine-naloxone dose, the average physician reported a mean dose of 13.4 mg (SD = 4.2) for stable patients. The most common average dose for stable patients was 14–16 mg, reported by 44.9% of the sample. Regarding maximum dose for stable patients, the mean was 21.5 mg (SD = 6.2). About half of physicians reported the maximum dose that they would prescribe to stable patients was 18–24 mg (51.5%), but 30.3% reported that the maximum dose they would prescribe was 16 mg.

Table 3
Attributes and levels of conjoint vignettes with part-worth utilities for frequency of office visits (Rating 1) and dose adjustments of buprenorphine-naloxone (Rating 2).

Attribute	Levels within the Attribute	Rating 1 Part-worth Utility (Standard Error)	Rating 2 Part-worth Utility (Standard Error)
Current daily dose	8 mg	−.222 (.094)	.930 (.056)
	16 mg	.039 (.110)	.158 (.066)
	24 mg	.182 (.110)	−1.088 (.066)
Pattern of urine drug test results, opioid blockade, and recent benzodiazepine use	Urine drug test (UDT) is usually opioid+; pt reports continued euphoric effects from illicit opioid use	.609 (.110)	.732 (.066)
	UDT occasionally opioid+ & pt reports no euphoria from illicit opioid use; UDT recently illicit benzodiazepine+	.101 (.110)	−.440 (.066)
	UDT occasionally opioid+ & pt reports no euphoria from illicit opioid use	−.710 (.094)	−.292 (.056)
History of intravenous use and current intravenous use	Has never injected opioids, and today has no visible track marks	−.479 (.094)	−.244 (.056)
	Primary route has been intravenous, and today has no fresh track marks	−.213 (.110)	−.045 (.066)
	Primary route has been intravenous, and today has fresh track marks	.691 (.110)	.289 (.066)
Previous office visit attendance	Attended previous office visit with you	.004 (.070)	−.012 (.042)
	Rescheduled previous office visit with you at the last minute	−.004 (.070)	.012 (.042)
Adherence to recommended counseling	Adherent to recommended counseling	−.229 (.070)	.022 (.042)
	Non-adherent to recommended counseling	.229 (.070)	−.022 (.042)
Method of payment for office visits	Has Medicaid to pay for office visits with you	.044 (.094)	.019 (.056)
	Has private insurance to pay for office visits with you	−.118 (.110)	.042 (.066)
	Is paying out-of-pocket (cash) for office visits with you	.074 (.110)	−.061 (.066)
Current frequency of office visits	Visits (with you) scheduled once a month with 30 days of bup/nx prescribed	.589 (.070)	.066 (.042)
	Visits (with you) scheduled every two weeks with 14 days of bup/nx prescribed	−.589 (.070)	−.066 (.042)
Constant		7.664 (.084)	5.455 (.051)

Notes. Part-worth utilities were calculated based on physicians' responses to Patients 1-16. Part-worth utilities, similar to regression coefficients, are indicative of the influence of that specific level on physicians' responses as well as the direction of the association. Rating 1 asked respondents, "How would you adjust the frequency of office visits (with you, the treating physician) for this patient?" on a 0–10 scale with anchors of 0 = definitely decrease the frequency of office visits, 5 = make no change, and 10 = definitely increase the frequency of visits. Rating 2 asked, "How would you adjust the daily milligram dose for this patient?" with response options ranging from 0 to 10 where the scale anchors were 0 = definitely decrease the dose (mg/day), 5 = make no change to the dose, and 10 = definitely increase the dose (mg/day).

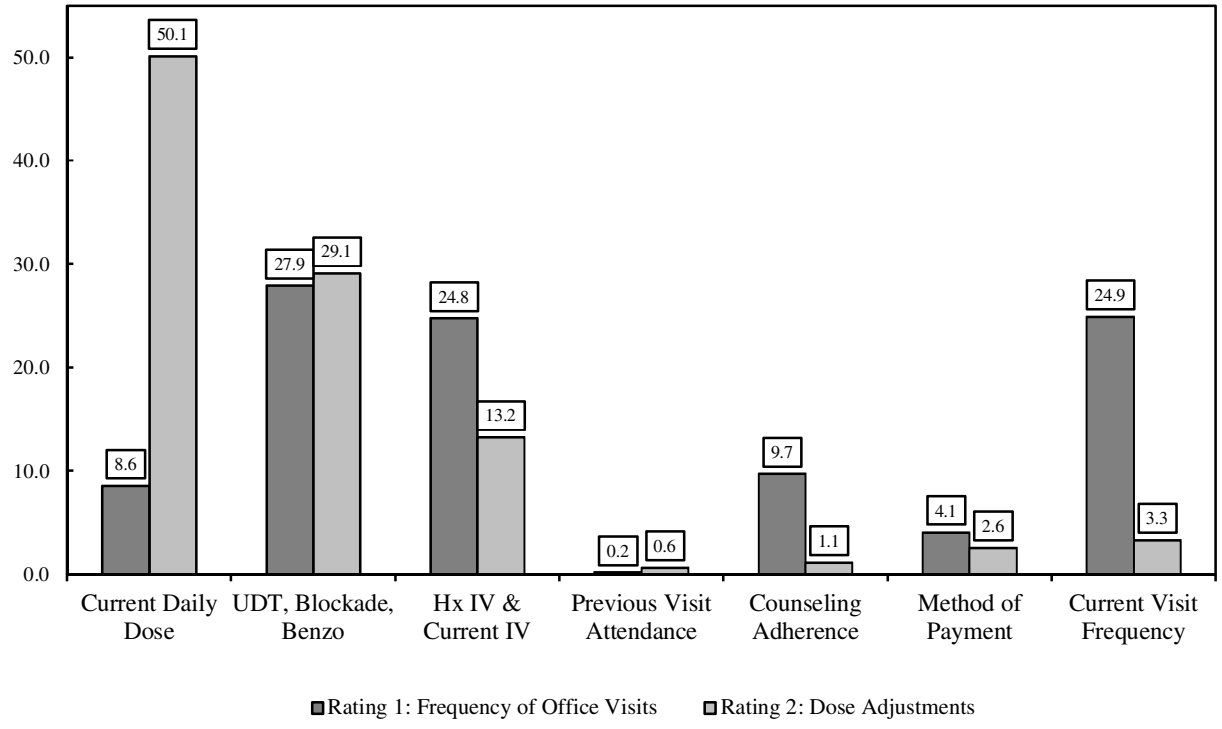

Fig. 1. Average relative importance scores of seven attributes in changes in the frequency of office visits and dose adjustments of buprenorphine-naloxone.
Notes. Because average relative importance scores always sum to 100, the magnitudes of these scores can be compared across the attributes.

Table 4
Physicians' self-reported office visit and dosing practices.

	% (N)
Typical frequency of office visits for stable patients after 2 months of treatment	
Every other week or more frequently	12.4% (92)
Once a month	73.0% (544)
Less than once a month	14.6% (109)
Typical frequency of office visits for unstable patients (i.e., ongoing substance use) after 2 months of treatment	
Every week	35.0% (261)
Every other week	39.8% (297)
Once a month or less frequently	18.9% (141)
Patient would be discharged	6.3% (47)
Average dose for stable patients	
8mg or less	20.6% (152)
10-12mg	28.1% (207)
14-16mg	44.9% (331)
Greater than 16mg	6.5% (48)
Maximum dose	
Less than 16mg	6.1% (45)
16mg	30.3% (222)
18-24mg	51.5% (378)
Greater than 24 mg	12.1% (89)

Notes. Due to rounding error, some percentages may sum to more than 100%.

4. Discussion

In this study of physician decision-making, we found US physicians were generally willing to increase the frequency of office visits in response to changes in patient treatment progress depicted in vignettes. For office visits, the most important attributes were UDT results/opioid blockade, signs of recent intravenous use, and the current visit schedule. The overall mean response across the vignettes for dose adjustments tended towards making no dose adjustments, although there was variation in scores for specific patient vignettes, indicating some support for changing the dose. UDT results/opioid blockade and recent intravenous use were important attributes for dose adjustments, but the patient's current dose had the largest importance score.

In the self-reported survey data on typical practices, office visits were less frequent when patients achieved stability. Monthly visits were the norm, and about one in six physicians reported seeing stable patients even less frequently. This subset of physicians using a less than monthly schedule is consistent with an analysis of Pennsylvania Medicaid claims data that revealed that nearly one-quarter of prescriptions did not have an associated physician visit in the preceding 30 days (Gordon et al., 2015). Similarly, the limited proportion who saw stable patients more frequently than once a month aligns with the previous finding of Yang et al. (2013) who found only about one-third of physicians saw patients more frequently than once a month.

Both the conjoint analysis and self-report data point to how US physicians use office visits to respond to patients with signs of clinical instability. In the conjoint analysis, willingness to see the patient more frequently was positively associated with signs of insufficient opioid blockade, recent intravenous use, and a current schedule of monthly visits. Similarly, the majority of physicians reported that either weekly or biweekly visits were their typical strategy for scheduling office visits for patients with ongoing opioid and other drug use. As noted by LaBelle et al. (2016), this method of individualizing treatment in response to clinical progress is consistent with how other chronic conditions are managed. What remains unclear is the extent to which this strategy of intensifying the frequency of office visits improves the likelihood of treatment retention and subsequent reduction in opioid use, as RCTs of buprenorphine-naloxone treatment have not examined how the timing and frequency of medical management via office visits may impact clinical outcomes (Carroll and Weiss, 2017).

With regard to the outcome rating for dose adjustment, the part-worth utilities indicated that physicians were more willing to increase the dose when it was 8 mg and more willing to reduce the dose when it was 24 mg. To some extent, these adjustments are supported by previous research. Some chart reviews have shown that lower doses, especially 8 mg or less, are associated with treatment dropout and shorter duration of treatment (Kapuganti et al., 2017). A clinic-based study that examined a Medicaid-mandated dose reduction showed that patients who had been at doses above 16 mg and had their dose reduced (without consideration of clinical progress) had lower retention than non-Medicaid patients who were at high doses and did not experience a mandated dose reduction (Accurso and Rastegar, 2016). Higher doses decrease the odds of dropout (Gryczynski et al., 2014; Hser et al., 2014; Jacobs et al., 2015), and a meta-analysis of RCTs indicated that doses of at least 16 mg were positively associated with study completion (Fareed et al., 2012). However, analyses of pharmacy claims data have yielded conflicting results, with some studies finding that higher doses improve retention (Clark et al., 2014; Lo-Ciganic et al., 2016) while others have reported no association between dose and retention (Manhapra et al., 2018; Shcherbakova et al., 2018). Furthermore, it is important to consider both physicians' judgments about dose adequacy and patient preferences regarding the dose, as there is some evidence that clinical outcomes are worse when physicians judge the dose as clinically inadequate but patients desire adjustment to a moderate dose (Alcaraz et al., 2018). Patients reporting their dose is inadequate are more likely to report ongoing opioid use (Gonzalez-Saiz et al., 2018).

Perhaps some of these mixed findings in observational studies of dose and retention reflect analytic models that do not include measures of clinical instability, such as repeated opioid-positive UDTs during the treatment episode, as covariates. In addition to current dose, our conjoint analysis demonstrated that physicians were responsive to signs of inadequate opioid blockade (as indicated by UDT results that were usually positive and patient-reported euphoria) and evidence of recent injection when considering upward adjustments in dose. More research is needed about whether physicians' responses to signs of clinical instability, particularly by adjusting the dose, can re-stabilize the patient and subsequently improve treatment retention.

In these vignettes, the attribute about adherence to recommended counseling had little impact on the two outcome ratings. This sample of buprenorphine-prescribing actually strongly endorsed the value of psychosocial interventions as part of the treatment process during our baseline survey (Lin et al., 2019), although counseling adherence was not a major decision-making factor in these vignettes. It may be that the levels for this attribute were too vague, as the vignettes simply noted whether the patient was adherent to recommended counseling, without specifying the evidence of adherence (e.g., patient self-report) or the intensity of or rationale for counseling requirements that had been recommended to the patient. Furthermore, the role of psychosocial supports in buprenorphine treatment continues to be debated. Studies of interim buprenorphine without formal counseling have shown reductions in opioid use (Dunlop et al., 2017; Sigmon et al., 2016). The WHO practice guidelines point to the importance of psychosocial interventions (World Health Organization, 2009), but the more recent ASAM guidelines and systematic reviews note that there is not strong evidence for an incremental benefit of psychosocial treatment beyond medical management (American Society of Addiction Medicine, 2015; Carroll and Weiss, 2017; Dugosh et al., 2016).

This study has several limitations that warrant consideration. First, only buprenorphine-prescribing physicians in the US were recruited, so it is unknown if these findings would generalize to other medical professionals who can now obtain the US waiver. Furthermore, generalizations cannot be drawn to practitioners outside the US where models of care are different. For example, supervised dosing is used in some countries, such as Australia where patients may receive their supervised doses in pharmacy settings (Yokell et al., 2011). The comparative effectiveness of supervised dosing versus take-home medication strategies remains unclear (Saulle et al., 2017). In this sample of US physicians, most were in office-based practice where supervised dosing was

unlikely.

Additionally, conjoint analysis is limited by the factors presented in the vignettes. Other factors, such as information about patients' medication adherence as measured by urine test results, patients' perceptions of dose adequacy, and patient-reported side effects may influence physicians' decision-making about adjustments to treatment. Future research seeking to apply this methodology to the study of dose and office visit adjustments should retain the key characteristics identified in this study while adding additional factors. This approach to a future study could address whether other patient factors are more or less important in terms of decision-making than the factors with the largest importance scores in the current study. In addition, research is needed on how physician and treatment setting characteristics may be related to decision-making and how these decisions affect critical patient outcomes, such as retention in treatment and mortality.

Tailoring treatment to individual patients, particularly in response to indicators of clinical progress, is an important element of patient-centered care involving buprenorphine pharmacotherapy. In this sample of US physicians, responses to patient vignettes indicated that physicians were willing to individualize treatment by adjusting the frequency of office visits but were somewhat less willing to adjust buprenorphine-naloxone doses in response to clinical indicators at doses of 16 mg or more daily. Given these practice patterns, more research is needed to examine the impact of dose and office visit adjustments on enhancing treatment retention and increasing the likelihood of OUD remission.

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Contributors

All authors are responsible for this reported research. H. Knudsen, M. Lofwall, S. Walsh, and J. Studts collaborated in the design of the patient vignettes. H. Knudsen estimated the statistical models and drafted the initial manuscript. M. Lofwall, L. Lin, S. Walsh, and J. Studts contributed to drafting the manuscript and interpreting the findings. All authors have reviewed the manuscript, revised its content, and have approved the final manuscript as submitted.

H. Knudsen, L. Lin, and J. Studts have no competing interests to declare. In recent years, M. Lofwall has received contract funding to support research from Braeburn Pharmaceuticals (which has developed a buprenorphine product), has provided consultation to Braeburn, CVS Caremark, and Indivior (which manufacture buprenorphine products), and has received honoraria from PCM Scientific, which received unrestricted educational grant funds from Reckitt Benckiser (now Indivior), for work in developing and presenting educational talks on opioid use disorder. Related to buprenorphine, S. Walsh has received research funding, consulting fees, and travel support from Braeburn and Camurus as well as travel support and honoraria from Indivior. She has also received consulting fees from Lilly, Inc., Pfizer, Brainsway, KemPharm, World Meds, INSYS and Daiichi-Sankyo in the last three years.

Declaration of Competing Interest

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