Journal of
Addiction Research & Therapy
ISSN: 2155-6105

Matos Santana et al., J Addict Res Ther 2017, 8:2
DOI: 10.4172/2155-6105.1000315

Review Article OMICS International

Risk/Benefit Discussion of Alcohol Use Disorder Medications: Behavioral Economic Considerations and General Recommendations

Teofilo Enrique Matos Santana[1*], **Mark Greenwald**[2] **and Marc I Rosen**[1]

[1]*Yale University School of Medicine, New Haven, Connecticut, USA*

[2]*Department of Psychiatry and Behavioral Neurosciences, Wayne State University School of Medicine, Department of Pharmacy Practice, Eugene Applebaum College of Pharmacy and Health Sciences; Wayne State University, Detroit, MI, USA*

[*]**Corresponding author:** Teofilo Enrique Matos Santana, Yale New Haven Hospital, New Haven, USA, Tel: 475-227-6646; E-mail: Teofilo.matossantana@yale.edu

Received date: February 08, 2017; **Accepted date:** March 24, 2017; **Published date:** March 31, 2017

Abstract

Background: Despite the development of several relatively safe and effective medications to treat alcohol use disorder (AUD), underutilization of these medications continues to be a challenge. With other factors, judgments about medications' risks and benefits can influence prescribers' practices and patients' acceptance of these medications.

Objective: Describe how behavioral economic principles and presentation of risks/benefits of AUD medications can impact these medications' utilization and suggest guidelines for how prescribers should describe these medications to patients.

Methods: Literature selected by the authors was used in this commentary and formulation of guidelines. Results: Behavioral economic principles relevant to judging risks and benefits of AUD medications include salience, recency, the halo effect, narrative thinking, avoiding cognitive dissonance, and patients' interoceptive effects. Benefits of reduced alcohol use may be too abstract without elaboration. Medications are more likely to be taken by patients who envision their benefits as salient, prompt, and consistent with other ideas they have about their alcohol use and/or tailored to their psychological state. Explaining risks and benefits using established quantitative and qualitative terms has predictable effects on patients' perceptions. Risk/benefit discussion should be bi-directional between patient and provider, personalized to issues valued by each patient, and tailored to the individual's alcohol-induced state. We propose methods to improve information transfer and reduce biased decision making.

Conclusion: Whether and how a risk/benefit discussion of AUD medications is conducted can influence utilization of these medications.

Keywords: Addiction; Utilization; Alcohol use disorder; Risk/benefit; Medication; Therapy

Introduction

Data from a recent national epidemiologic study indicate that 14% of the United States (US) population meet DSM-5 criteria for a current alcohol use disorder [AUD] [1]. Several relatively effective and safe medications have been developed to treat people with AUD [2-4]. To date, the US Food and Drug Administration (FDA) have approved four medications for the indication of reducing heavy alcohol drinking or promoting abstinence: orally administered disulfiram, naltrexone and acamprosate and injectable sustained-release naltrexone. In addition to these approved medications, physicians have prescribed other medications off-label for the purpose of reducing heavy alcohol use. FDA phase II randomized placebo-controlled trials have found efficacy for reducing heavy drinking or promoting abstinence for gabapentin [5-7] and topiramate [8-13]; baclofen was efficacious in some trials [14-16], but not in others [17,18].

Use of AUD pharmacotherapy varies considerably across locales, in part, due to system-level barriers such as differential access to these medications via formularies [19]. Surveys during the past 15 years have indicated that only 2-12% of AUD patients received pharmacotherapy [20-22], despite some increases over time [23]. The likelihood of a person with AUD being prescribed pharmacotherapy is much lower than the rate of someone with depression being prescribed an antidepressant [23,24].

There are numerous challenges translating the modest efficacy of these agents into real-world use. Individual patients may have limited coping and recovery skills and prefer psychosocial approaches to AUD medications for their AUD treatment [25]. A neurobiological framework is another way to explain limitations some patients' reluctance to adopt and adhere to treatment; e.g. neuroadaptation in the brain that determines motivation may cause avoidance of AUD medications [26]. Additionally, psychosocial factors including system of care and pharmacy formularies influence adoption of and adherence to AUD medications.

Another approach to better understand utilization of AUD medications is by analyzing the way in which prescribers and patients weigh risks and benefits, and how this discussion is presented in a way that encourage patients to take a given medication. The most commonly reported barriers among providers to prescribing AUD medications-lack of knowledge and lack of confidence in effectiveness of the drug [19,20,27]-reflect provider (mis)judgements about these medications' risks and benefits. Another reported reason for under

prescribing-lack of demand by patients [20] also reflects a risk/benefit (mis)calculation.

A prescriber's risk/benefit analysis should mediate whether to prescribe a medication to a patient, and the patient's understanding of risks and benefits is likely to determine whether a patient will agree to take the prescribed medication. Behavioral economists have described how perceived gains (benefits) and losses (risks) impact decision making [28]. These principles are applicable to AUD pharmacotherapy decision-making.

Herein we suggest that it is essential for prescribers to have a carefully crafted risk/benefit explanation to present to patients. We begin by applying an extensive literature from behavioral economics about how people more generally understand potential gains and losses to how the risks and benefits of AUD pharmacotherapy are understood. We then describe the modalities used to present risks and benefits. Based on this review, we make recommendations for presenting AUD pharmacotherapies to patients, considering each patient's particular characteristics including health literacy.

Importance of Framing Risk/Benefit Discussion for AUD Medication Utilization

Table 1 list psychological principles about how potential gains and losses are weighted (by prescribers and patients) that are particularly salient for AUD pharmacotherapy.

Principle	Explanation	Example of principle applied to AUD pharmacotherapy
Recency/Salience	More recent, vivid events have a disproportionate impact on decision making [1].	Side effects that occur to a person that the provider or the patient knew (compared with an anonymous patient) have a disproportionate impact on decision-making and can lead to overestimation of the risk.
Avoiding cognitive dissonance	Tendency to hold ideas/beliefs that are consistent with one's actions.	Prescribers lacking knowledge about naltrexone believed that patients were not interested in it [2]. Thus prescribers' beliefs about patients' attitudes were congruent with their not learning about naltrexone.
Halo effect	Attributes are not judged separately. Features of an object influence judgment about other features (e.g. someone who is attractive is also perceived to be nice) [3].	Prescribers make medications' risks and benefits correlate with each other in experimental paradigm [4]. Thus, patients' general attitudes towards a medication determine their weighing of individual features.
Use of schemas instead of deductive reasoning	Information is processed using mental shortcuts, preconceived ideas and ideas about how things are linked (e.g. narratives) [5]. This can result in perceiving two events that occur sequentially by chance as being causally related to each other.	People who believe addiction is caused by personal weakness hold a belief that may not support their taking AUD medications.
Framing effects (e.g. loss aversion)	The displeasure associated with a loss is greater than the pleasure associated with a gain of the same amount [6]. Therefore, when the more certain choice is a substantial loss, individuals will be risk-seeking.	People who perceive their alcohol use to be harming them should be more willing to gamble on taking a medication to avoid certain loss (continue to drink and its consequences), even though the medication may have risks.
Influence of interoceptive stimuli	Decision-making is impacted by one's current physical and psychological state [7,8].	Signs and symptoms of AUDs impact decision-making, e.g. people made anxious by alcohol withdrawal worry more (are more anxious about) side effects.

Table 1: Psychological principles impacting risk/benefit perceptions.

The following psychological principles shed light on the decision-making that influences prescribers' utilization and patients' acceptance of medications. It is noteworthy that these behavioral economic principles can apply to any medication; however, we applied them to the specific settings and actors in AUD medication use.

Recency/salience

Recent and/or vivid events disproportionately impact decision-making [29,30]. A study using case scenarios and a computerized analytic model to evaluate physician decision-making concerning antihypertensive medications showed that individuals tend to anchor their decisions based on recent and/or salient experiences and suggested that the occurrence of a medication's adverse effect could influence a prescriber to abandon an useful therapeutic agent even when the likelihood of this adverse effect was rare [31]. These can lead the physician to overestimate the probability of a recent versus a distal event, and to overestimate the likelihood of vivid events compared to less distinct ones. The effects of these biased responses were corrected when physicians were given probability estimates of the efficacy and adverse effects of the medications, and their decisions became more consistent with the computerized analytic model [31]. Unfortunately, side effects of AUD pharmacotherapy can be vivid, whereas reductions in alcohol use may not be as vivid. For example, the possibility of someone taking naltrexone not being able to respond to opioid analgesics is arguably not particularly important (and can be overridden) but it is vivid.

A common error in risk estimation is to overreact to a risk that receives substantial notoriety, such as the media attention given to a boxed warning; this reflects the bias towards considering information that is most available rather than that which is most relevant [29]. For example, FDA safety warnings about suicidal ideation in adolescents treated with SSRI antidepressants have resulted in reduced prescribing for youth with depressive disorders, but an unintended consequence has been a reduction in prescribing for other age groups for whom

there is no evidence of this adverse effect [32-34]. Other common errors are to overestimate very small risks and to underestimate large risks [35]. Additionally, a prescriber may inaccurately estimate the likelihood of a medication side effect based on the risk of other related medication that is familiar to him/her [29,35]. These particular biases can impact how prescribers select an AUD medication.

The principle of salience is particularly important for AUD pharmacotherapy and it applies to patients, too. For instance, disulfiram produces a very vivid adverse reaction when the patient ingests alcohol; therefore, many patients are unwilling to take it. Disulfiram was the only medication available to treat AUD for many years. Thus, when any other AUD medication is discussed, especially with an older patient, patients may be fearful of a disulfiram-type reaction.

Avoiding cognitive dissonance

As expected, a physician's perceptions of the effectiveness and safety of naltrexone have been shown to relate to his/her decision to prescribe [36]. In this particular study data was collected from a survey of US physicians in addiction treatment centers and it showed that physicians who did not prescribe naltrexone perceived the medication to have more side effects than those who did prescribe it and they reported patient's lack of interest as the main reason not to prescribe it. Prescribers who had access to accurate information about naltrexone were more likely to prescribe it. This study's findings suggest that believing patients are uninterested in naltrexone might be an attempt to rationalize the lack of knowledge about naltrexone and thus resolve the cognitive dissonance between prescribers' beliefs and actions. Unfortunately, people (including prescribers) tend to be overly confident about the extent and accuracy of their knowledge [29] and prescribers may change their understanding of the facts they are told to fit their firmly held, if inaccurate opinions, rather than changing the opinions.

Similar to physicians, patients also harmonize their beliefs, attitudes and decision-making to make them consistent with each other. For example, patients' positive beliefs about bupropion to facilitate smoking cessation were related to greater intentions, motivations, confidence and desire to quit smoking, as well as better treatment adherence [37].

Halo effect and narrative thinking

Individuals form general attitudes towards the potential gains and losses of a course of action, rather than mathematically weighing individual features [38,39]. A compelling demonstration that judgment of risk and benefit are not simply added mathematically is that multiple studies have found that judgments of a given treatment's risks and benefits are inversely correlated.

Activities that individuals judged to be high-risk also tended to be judged low-benefit and vice versa, as if a global judgment (halo) leads to a medication being judged as good or bad, and the judgment of risks and benefits is adjusted to better match the gestalt view of the medication. For example, students rated radiation therapy to be high-risk and low-benefit, whereas vaccines were judged to be high-benefit and low-risk, even though evidence indicates that radiation therapy has substantially greater benefit because it can cure cancer, an otherwise fatal disease [39]. This psychological study showed how perceived risk and benefit were almost unrelated when the risk level was perceived to be low or moderate; however, when the risk increased, the perceived benefit dropped substantially [39]. Applying these principles to the present context, it seems likely that when a prescriber emphasizes that the risk of AUD medication is high; this will reduce the patient's perception that the medication is effective.

When processing complex information (such as weighing risks and benefits), people are inclined to take mental shortcuts, i.e., engage in schematic thinking [40]. These mental heuristics include fitting the novel information into a narrative that incorporates their pre-existing ideas. However, this can lead to several unintended biases. For instance, in a discrete-choice study that evaluated provider decision-making, when a theoretical AUD medication was assigned optimal attributes, physicians still would prescribe it to only 53% of the patients [41].

This finding suggests that factors other than medication attributes are biasing prescribers away from prescribing AUD medications. These biases may include the narrative belief that people who develop AUD did so by making bad choices. The belief that patients brought about their condition may be coupled with a belief they should "fix it" on their own. This narrative leaves little place for AUD medications.

Framing effect (gain and loss frames)

The way in which health information is presented influences people's treatment choices [28,42,43]. A physician's message when introducing treatment options can have a positive "gain" frame that focuses on the advantages of stopping the risky behavior (e.g. improved health and function by ceasing heavy drinking) or a negative "loss" frame that emphasizes the disadvantages of the status quo (e.g. worsening health due to continued heavy drinking). In other types of health scenarios, a positively framed message might present the benefits of the intervention (survival rate) whereas a negatively framed message might present the risks of the treatment intervention (mortality rate).

Alcohol cessation messages have, in several studies [42,44,45], been most effective when they emphasized the gains of stopping drinking. This observation has been explained by loss aversion. The literature on decision-making suggests that individuals tend to be risk-averse (decrease risky behavior) when considering gains but are generally more willing to continue risky behavior when faced with potential losses. Therefore if a gain is made salient, people will tend to avoid risk, and when the loss is made important individuals will tend to be risk-seeking [28]. Thus, prescribers may consider the patients' perspective on whether the consequence of the status quo (without medication) is seen by the patient as a likely loss or gain.

Another finding impacting choice framing is that people with AUD discount the value of future gains more than non-affected controls [46], which suggests they are particularly likely to devalue gains that only will emerge far in the future.

Influence of interoceptive stimuli

Biological and psychological states stimulate ("prime") people to think of things related to these states [26,47]. This would be expected to manifest itself in patients' response to proffered medications being impacted by substance-induced endogenous states. The state of substance intoxication and withdrawal, mood and arousal state can affect the interpretation of AUD risk/benefit.

Unfortunately, states associated with alcohol use such as withdrawal and craving can make alcohol use seem more appealing. The

implication for an AUD risk/benefit discussion is that a patient who is presently craving alcohol is primed to hear the risks of AUD medications as being more salient and the benefits as less alluring. In multiple other domains, physiological conditions impact preference. High arousal (which may be associated with positive or negative affect) is associated with risk taking and low arousal with risk aversion [48]. In a different scenario, Ariely and Lowenstein found that risky and morally questionable behaviors were considered more attractive when male participants were sexually aroused than when they were not [49].

The physiological and structural changes that alcohol causes in the brain can impair rational decision-making. Decisions can become more impulsive, and more focused on the short-term at the expense of longer-term considerations [50].

Making the Numbers Understandable: Alternative Ways for Prescribers to Present Risks and Benefits

Formats of medication risk presentation

The upper half of Table 2 summarizes the common formats used to present the likelihood of harms: adjectives (e.g. "common" or "rare"), numbers, and graphs/pictures [51]. Qualitative formats tend to be easily grasped, but they are imprecise leading to overestimation of the risk. For example, patients who were told that a side effect of their lipid-lowering medication was "common," which is standardized in European Union (EU) guidelines as having an estimated frequency of 2.5%, thought the likelihood of the side effect was in fact much higher (34%) [52]; and they similarly estimated that a side effect described as "rare" (0.04% per EU verbal descriptors guidelines) occurred more frequently (18%).

Patients prefer numerical representations of the likelihood of adverse events even when the numerical format (frequency, percentage) is more difficult to understand [29,51-53]. Simple frequency (e.g. 1 out of 50) is the easiest number to understand, followed by percentage [51]. Visual representation (pictograph) of frequencies-using stick figures to represent the numbers of patients affected and unaffected by side effects-results in better comprehension and recall of information [51].

What is being presented	Format	Illustration	Impact on patient's decision	Recommendation
Likelihood of side effects	Qualitative (verbal): e.g. "common" or "rare"	Suicidal ideation is a rare side effect of naltrexone	Patients think these words connote more risk than providers intend to convey	Use when exact probability of outcome is unknown
				Use to describe the nature of the side effect
	Quantitative (numeric):			
	Frequency "1 in 100"	10 in 100 patients taking naltrexone experience nausea	Can be difficult to understand	Use single frequencies when available
	Percentage "1%"	10% of patients taking naltrexone experience nausea	Single frequency is generally the best understood	
	Graphic or pictures	Pictograph showing 100 patients taking naltrexone and 1 of them affected with suicidal thoughts	More salient, enhancing comprehension and recall of information	Use when available
Likelihood of efficacy	Absolute risk reduction	There were 15% fewer heavy drinking episodes in patients taking naltrexone comparing to placebo	Less biased but less intuitive to understand	Use as available

Table 2: Modalities for presenting risks and benefits.

Formats of medication benefit presentation

The formats used to present risks can also be used to present benefits. The lower half of Table 2 summarizes additional formats used to present the likelihood of benefits: absolute risk reduction, relative risk reduction, and number needed to treat. Absolute risk reduction is the absolute difference between the outcome rates of the experimental (e.g. medication) group and the control group. For example, if in a study of people who all drank heavily at enrolment, naltrexone is associated with a 40% likelihood of heavy drinking after 12 weeks and placebo is associated with a 55% rate, the absolute risk reduction is 55% minus 40% equals 15%.

Relative risk reduction indicates how much risk (e.g. persistent heavy drinking) is reduced in the experimental group compared to a control group, and thus incorporates the baseline rate into the calculation. Using the example above, the relative risk reduction would be a 15% reduction in drinking divided by a 55% reduction in the control group, equaling 27%. The number needed to treat refers to the number of patients who need to be treated, compared with a control, to get the desired outcome in one patient. Number needed to treat is calculated by dividing 1 by the absolute risk reduction (in this case, 1 ÷ 15%=7). In this example, 7 people would need to be treated to see a benefit. Studies consistently report that relative risk formats produce more favorable evaluation of treatments [54], perhaps because this format involves larger absolute numbers.

Recommendations

General considerations about risk/benefit ratio discussion

The following recommendations incorporate important elements from the shared decision-making model of care. This model is characterized by information and responsibility sharing between prescriber and patient, and by the patient's active engagement in discussing risks and benefits with the goal of optimizing a decision that is congruent with the patient's values and preferences [55,56]. This model has led to more accurate risk perceptions by patients, a greater number of decisions consistent with patients' values, and a reduced level of internal decisional conflict for patients [57].

It is important to present both risks and benefits of an indicated AUD medication systematically and thoroughly. Patients generally want to receive information about the benefits of their medications. In one representative study, patients in a focus group endorsed having benefits information placed in medicine leaflets, with some stating this procedure would increase their likelihood of taking the medication [53]. Medication risks are often not mentioned during medical encounters [29,58], despite the clear importance of doing so, both for patient safety and for ethical reasons (i.e., autonomy). When risks are discussed, usually they are described in non-specific qualitative formats that result in poor recall of the discussion by the patient [58].

Table 3 summarizes how to present risks and benefits to patients considering AUD medications.

Attributes to present to patients	Process/communication skills	Example
Pharmacological properties	Consider patient's health literacy so patient understands the message	"Naltrexone blocks pain receptors in your brain and cuts down craving for alcohol. People who take it spend fewer days drinking heavily. We can start with 50 mg once a day. It can help you drink less and help you be more available to your family. The medicine will help with some of the chemical problems that alcohol use has caused in your brain, but you also have to learn to do things that will help you lead a healthy life with less alcohol".
Efficacy	Discuss efficacy for different outcomes	
	Explain the benefits for the patient's specific complaints.	
Side effects	Relate side effects to patient's personal situation	"Naltrexone causes stomach upset and headache in 1 out of 10 patients. One out of 100 patients will develop suicidal thoughts and even more rarely, naltrexone can irritate the liver. We will monitor your liver with blood tests. If you have any of these problems, we will stop the naltrexone and that will almost always make the side effects go away".
	Discuss likelihood and permanence	
	Offer solutions for possible side effects	
	Show expertise and be available	

Table 3: Presentation of risk/benefit ratio of AUD medications.

When presenting information to someone with short-term memory deficits often seen with chronic alcohol use [59], providers may present the information more than once or present written materials that the patient can refer to later. Another way to bolster the patient's decision-making capacity, and perhaps their recovery-oriented choosing, is to conduct the risk/benefit discussion with someone whom the patient trusts to help the patient weigh these considerations. As has been shown for a variety of medical discussions [60,61], the presentation of risk/benefit will be better received if it is a bilateral discussion, rather than a speech from the prescriber.

Presentation of AUD medication attributes

Pharmacological properties

The physician will explain the attributes of the medication including the name, class and mechanism of action, taking into account the patient's health literacy. Avoiding medical jargon will enhance the patient's understanding. The medication recommended and its indication should be personalized to the patient's particular needs. The patient will want to know the route of administration and dosing.

Efficacy

The medication's efficacy is better understood when it is stated clearly, not only for abstinence but also for other drinking outcomes (e.g. heavy drinking days, improved liver function). This is consistent with recent changes in FDA guidance on the design of medication clinical trials that emphasize reduction in heavy drinking over total abstinence [2]. If the medication's benefits accrue at some delay after starting treatment, this should be explained.

Combining the medication's benefits with a plan for psychosocial interventions can ensure better outcomes. There are cognitive-behavioral skills (relapse prevention strategies) that will help in conjunction with the medication.

Side effects

It is necessary to disclose any regulatory warning. Clarification of permanence (side effect lasting a week or permanent), timing (at the beginning of treatment or later during treatment), and the probability of the expected outcome are of great importance [29]. The patient will appreciate if he is informed about appropriate measures to be taken to prevent or manage any adverse event. Monitoring vital signs, blood tests, and mood can minimize adverse events.

It is important that providers consider the effects of verbal, numerical or graphical representation in relation to the patient's perception of the level of risk. They can do so by choosing a risk presentation format that the patient is most likely to understand. It is important to tell the patient about side-effect management strategies they can use on their own and those for which they should call the prescriber.

The risk of leaving AUD untreated is part of the risk discussion [29]. Unchecked AUD is associated with significant morbidity and mortality and declining an AUD medication risks the psychosocial and medical consequences of drinking.

Personalization of risk/benefit ratio

A risk/benefit discussion tailored to patients' needs is optimal [29]. For example, if a patient is experiencing insomnia, in addition to urges that foreshadow relapse to drinking, the patient may prefer an AUD medication that is sedating and can be taken at night (e.g. gabapentin). This approach also takes advantage of the previously mentioned observation that AUD patients are particularly likely to value immediate (versus deferred) benefits. For other patients with ambivalence about the goal of reducing alcohol use and resistance to take AUD medications, the prescriber might use Motivational Interviewing to promote change. Prescribers can also personalize the description of side effects that are highly unlikely in a particular patient, e.g. "Naltrexone produces undesirable symptoms in patients taking opioid pain relievers, however, you are not likely to be affected by this because you don't have a disease that requires opioid pain medications". Conversely, providers will understand the risks a patient will be particularly sensitive to. For example, a patient with a cognitively demanding job may consider the risk of cognitive slowing from topiramate to be extremely distressing.

It is not uncommon for patients to form unrealistic expectations about a medication's effects. This issue has been studied with medications that promote weight loss [62]. Patients' average expectations of weight loss pharmacotherapies are that 35% of body weight will be lost, which can lead to disappointment and stopping the medication because it "isn't working." In the context of AUD pharmacotherapy, a pivotal study of naltrexone coupled with either therapy targeted at coping with relapses or supportive therapy, the patients who were taught coping skills were less likely to relapse to alcohol use [63]. Therefore, when presenting the attributes of naltrexone, therapists aiming to minimize relapses can clarify that the medication alone is not expected to stop alcohol craving completely and that a slip to drinking does not represent a treatment failure.

Summary

Inferences from cognitive psychology and behavioral economic choice theory suggest that how risk-benefit information is presented significantly affects choices that patients and providers make about the use of AUD medications [64]. Herein, we have proposed a framework for risk/benefit discussion in the setting of AUD. Further studies are necessary to describe how prescribers currently understand the risks and benefits of each AUD-targeting medication, how they communicate them to patients, and how patients perceive the risks and benefits. Studies of structured interventions that present this information will be important to identify the best ways to ensure that patients are informed, and may change aggregate decision-making in the direction of more prescribing, initiation of, and adherence to AUD medication they communicate them to patients, and how patients perceive the risks and benefits. Studies of structured interventions that present this information will be important to identify the best ways to ensure that patients are informed, and may change aggregate decision-making in the direction of more prescribing, initiation of, and adherence to AUD medications.

Conflicts of Interest

The authors report no relevant financial conflicts.

References

1. Grant BF (2015) Epidemiology of DSM-5 alcohol use disorder: Results from the national epidemiologic survey on alcohol and related conditions III. JAMA Psychiatry 72: 757-66.
2. Anton RF (2006) Combined pharmacotherapies and behavioral interventions for alcohol dependence: The COMBINE study: A randomized controlled trial. JAMA 295: 2003-2017.
3. Jonas DE, Amick HR, Feltner C, Bobashev G, Thomas K, et al. (2014) Pharmacotherapy for adults with alcohol use disorders in outpatient settings: A systematic review and meta-analysis. JAMA 311: 1889-1900.
4. Skinner (2014) Disulfiram efficacy in the treatment of alcohol dependence: A meta-analysis. PLoS ONE 9: e87366.
5. Anton RF, Myrick H, Wright TM, Latham PK, Baros AM, et al. (2011) Gabapentin combined with naltrexone for the treatment of alcohol dependence. Am J Psychiatry 168: 709-717.
6. Brower KJ (2008) A randomized double-blind pilot trial of gabapentin versus placebo to treat alcohol dependence and comorbid insomnia. Alcohol Clin Exp Res 32: 1429-1438.
7. Mason BJ, Quello S, Goodell V, Shadan F, Kyle M, et al. (2014) Gabapentin treatment for alcohol dependence: A randomized clinical trial. JAMA Intern Med 174: 70-77.
8. Baltieri DA, Daró FR, Ribeiro PL, de Andrade AG (2008) Comparing topiramate with naltrexone in the treatment of alcohol dependence. Addiction 103: 2035-2044.
9. Batki SL (2014) Topiramate treatment of alcohol use disorder in veterans with posttraumatic stress disorder: A randomized controlled pilot trial. Alcohol Clin Exp Res 38: 2169-2177.

10. Blodgett JC, Del Re AC, Maisel NC, Finney JW (2014) A meta-analysis of topiramate's effects for individuals with alcohol use disorders. Alcohol Clin Exp Res 38: 1481-1488.
11. Johnson BA, Ait-Daoud N, Bowden CL, DiClemente CC, Roache JD, et al. (2003) Oral topiramate for treatment of alcohol dependence: A randomised controlled trial. Lancet 361: 1677-1685.
12. Johnson BA, Rosenthal N, Capece JA, Wiegand F, Mao L, et al. (2007) Topiramate for treating alcohol dependence: A randomized controlled trial. JAMA 298: 1641-1651.
13. Martinotti G (2014) Low-dose topiramate in alcohol dependence: A single-blind, placebo-controlled study. J Clin Psychopharmacol 34: 709-715.
14. Addolorato G (2011) Dose-response effect of baclofen in reducing daily alcohol intake in alcohol dependence: Secondary analysis of a randomized, double-blind, placebo-controlled trial. Alcohol Alcohol 46: 312-317.
15. Addolorato G (2007) Effectiveness and safety of baclofen for maintenance of alcohol abstinence in alcohol-dependent patients with liver cirrhosis: Randomised, double-blind controlled study. Lancet 370: 1915-1922.
16. Leggio L (2012) Baclofen promotes alcohol abstinence in alcohol dependent cirrhotic patients with hepatitis C virus (HCV) infection. Addict Behav 37: 561-564.
17. Garbutt JC, Kampov-Polevoy AB, Gallop R, Kalka-Juhl L, Flannery BA (2010) Efficacy and safety of baclofen for alcohol dependence: A randomized, double-blind, placebo-controlled trial. Alcohol Clin Exp Res 34: 1849-1857.
18. Ponizovsky AM (2015) Baclofen as add-on to standard psychosocial treatment for alcohol dependence: A randomized, double-blind, placebo-controlled trial with 1 year follow-up. J Subst Abuse Treat 52: 24-30.
19. Oliva EM (2011) Barriers to use of pharmacotherapy for addiction disorders and how to overcome them. Curr Psychiatry Rep 13: 374-381.
20. Harris AH (2013) Pharmacotherapy for alcohol dependence: Perceived treatment barriers and action strategies among veterans' health administration service providers. Psychol Serv 10: 410-419.
21. Iheanacho T, Issa M, Marienfeld C, Rosenheck R (2013) Use of naltrexone for alcohol use disorders in the veterans' health administration: A national study. Drug Alcohol Depend 132: 122-126.
22. Rubinsky AD (2015) Comparative utilization of pharmacotherapy for alcohol use disorder and other psychiatric disorders among US veterans health administration patients with dual diagnoses. J Psychiatr Res 69: 150-157.
23. Mark TL (2009) Alcohol and opioid dependence medications: Prescription trends, overall and by physician specialty. Drug Alcohol Depend 99: 345-349.
24. Knudsen HK, Abraham AJ, Roman PM (2011) Adoption and implementation of medications in addiction treatment programs. J Addict Med 5: 21-27.
25. Andréasson S, Danielsson AK, Wallhed-Finn S (2013) Preferences regarding treatment for alcohol problems. Alcohol Alcohol 48: 694-699.
26. Kranzler HR, Koob G, Gastfriend DR, Swift RM, Willenbring ML (2006) Advances in the pharmacotherapy of alcoholism: Challenging misconceptions. Alcohol Clin Exp Res 30: 272-281.
27. Thomas CP, Wallack SS, Lee S, McCarty D, Swift R (2003) Research to practice: Adoption of naltrexone in alcoholism treatment. J Subst Abuse Treat 24: 1-11.
28. Tversky A, Kahneman D (1981) The framing of decisions and the psychology of choice. Science 211: 453-458.
29. Bogardus ST Jr, Holmboe E, Jekel JF (1999) Perils, pitfalls, and possibilities in talking about medical risk. JAMA 281: 1037-1041.
30. Lau AYS, Coiera EW (2007) Do people experience cognitive biases while searching for information? J Am Med Inform Assoc 14: 599-608.
31. Carter BL (1993) Evaluation of physician decision making with the use of prior probabilities and a decision-analysis model. Arch Fam Med 2: 529-534.
32. Libby AM, Orton HD, Valuck RJ (2009) Persisting decline in depression treatment after FDA warnings. Arch Gen Psychiatry 66: 633-639.
33. Lineberry TW, Bostwick JM, Beebe TJ, Decker PA (2007) Impact of the FDA black box warning on physician antidepressant prescribing and practice patterns: Opening Pandora's suicide box. Mayo Clin Proc 82: 518-520.
34. Piening S (2012) Impact of safety-related regulatory action on clinical practice: A systematic review. Drug Saf 35: 373-385.
35. Fischhoff B, Bostrom A, Quadrel MJ (1993) Risk perception and communication. Annu Rev Public Health 14: 183-203.
36. Mark TL, Kranzler HR, Song X (2003) Understanding US addiction physicians' low rate of naltrexone prescription. Drug Alcohol Depend 71: 219-228.
37. Fucito LM (2009) Beliefs and attitudes about bupropion: Implications for medication adherence and smoking cessation treatment. Psychol Addict Behav 23: 373-379.
38. Wetzel CG, Wilson TD, Kort J (1981) The halo effect revisited: Forewarned is not forearmed. J Exp Soc Psychol 17: 427-439.
39. Alhakami AS, Slovic P (1994) A psychological study of the inverse relationship between perceived risk and perceived benefit. Risk Anal 14: 1085-1096.
40. Cheng PW, Holyoak KJ (1985) Pragmatic reasoning schemas. Cogn Psychol 17: 391-416.
41. Mark TL, Swait J (2003) Using stated preference modeling to forecast the effect of medication attributes on prescriptions of alcoholism medications. Value Health 6: 474-482.
42. Gong J, Zhang Y, Yang Z, Huang Y, Feng J, et al. (2013) The framing effect in medical decision-making: A review of the literature. Psychol Health Med 18: 645-653.
43. Fagley NS, Miller PM (1990) The effect of framing on choice. Pers Soc Psychol Bull 16: 496-510.
44. Gerend MCM (2008) Effects of message framing and temporal context on college student drinking behavior. J Exp Soc Psychol 44: 1167-1173.
45. Moxey A, O'Connell D, McGettigan P, Henry D (2003) Describing treatment effects to patients. J Gen Intern Med 18: 948-959.
46. Petry NM (2001) Delay discounting of money and alcohol in actively using alcoholics, currently abstinent alcoholics and controls. Psychopharmacology (Berl) 154: 243-250.
47. Naqvi NH, Bechara A (2010) The insula and drug addiction: An interoceptive view of pleasure, urges, and decision-making. Brain Struct Funct 214: 435-450.
48. Haim M (1994) Risk-taking, framing effects and affect. Organ Behav Hum Decis Process 57: 38-58.
49. Ariely DLG (2005) The heat of the moment: The effect of sexual arousal on sexual decision making. J Behav Dec Making 19: 87-98.
50. Bechara A, Damasio H (2002) Decision-making and addiction (part I): Impaired activation of somatic states in substance dependent individuals when pondering decisions with negative future consequences. Neuropsychologia 40: 1675-1689.
51. Burkell J (2004) What are the chances? Evaluating risk and benefit information in consumer health materials. J Med Libr Assoc 92: 200-208.
52. Knapp P, Raynor DK, Berry DC (2004) Comparison of two methods of presenting risk information to patients about the side effects of medicines. Qual Saf Health Care 13: 176-180.
53. Hamrosi K (2013) It's for your benefit: Exploring patients' opinions about the inclusion of textual and numerical benefit information in medicine leaflets. Int J Pharm Pract 21: 216-225.
54. Covey J (2007) A meta-analysis of the effects of presenting treatment benefits in different formats. Med Decis Making 27: 638-654.
55. Barry MJ, Edgman-Levitan S (2012) Shared decision making-pinnacle of patient-centered care. N Engl J Med 366: 780-781.
56. Charles C, Gafni A, Whelan T (1997) Shared decision-making in the medical encounter: What does it mean? (or it takes at least two to tango). Soc Sci Med 44: 681-692.

57. Stacey D (2014) Decision aids for people facing health treatment or screening decisions. Cochrane Database Syst Rev CD001431.
58. Kalet A, Roberts JC, Fletcher R (1994) How do physicians talk with their patients about risks? J Gen Intern Med 9: 402-404.
59. Grant I (1987) Alcohol and the brain: Neuropsychological correlates. J Consult Clin Psychol 55: 310-324.
60. Roter D (2000) The medical visit context of treatment decision-making and the therapeutic relationship. Health Expect 3: 17-25.
61. Roter D (2000) The enduring and evolving nature of the patient-physician relationship. Patient Educ Couns 39: 5-15.
62. Foster GD (1997) What is a reasonable weight loss? Patients' expectations and evaluations of obesity treatment outcomes. J Consult Clin Psychol 65: 9-85.
63. O'Malley SS, Jaffe AJ, Chang G, Schottenfeld RS, Meyer RE, et al. (1992) Naltrexone and coping skills therapy for alcohol dependence. A controlled study. Arch Gen Psychiatry 49: 881-887.
64. Redelmeier DA, Rozin P, Kahneman D (1993) Understanding patients decisions - cognitive and emotional perspectives. JAMA 270: 72-76.