Medical Research Archives

ESMED European Society of Medicine

OPEN ACCESS

Published: April 30, 2023

Citation: Margolin L, Margolin D, et al., 2023. Correlation between NARX Score and Food Addictive Behavioral Patterns in Chronic Pain Patients, Medical Research Archives, [online] 11(4). https://doi.org/10.18103/mra.v11i4.3727

DOI
https://doi.org/10.18103/mra.v11i4.3727

ISSN: 2375-1924

RESEARCH ARTICLE

Correlation between NARX Score and Food Addictive Behavioral Patterns in Chronic Pain Patients

Leon Margolin*, Daniel Margolin, Jeremy Luchins, Michelle Margolin and Sanford Lefkowitz

Comprehensive Pain Management Institute, LLC, Columbus, Ohio, USA

***Corresponding author:** Leon Margolin
Comprehensive Pain Management Institute, LLC (CPMI)
5245 E Main Street
Columbus, Ohio 43213
USA
www.cpmiohio.com

Funding
The author(s) received no financial support for the research, authorship and/or publication of this article.

ORCID iDs
Leon Margolin, MD, PhD https://orcid.org/0000-0002-0642-300X
Jeremy Luchins, PhD https://orcid.org/0000-0003-2806-6872

ABSTRACT
Setting and Objective. With still rising drug overdose deaths already at unprecedented alarming levels, reliable indicators of addiction and addiction-vulnerability are urgently needed. In the U.S., NARX scores are widely accepted as providing objective measures / predictors of drug-addiction risk. NARX scores are deemed especially useful when informing a broad patient-profile. Such profiles may to good advantage be enriched by patients' answers to standard health questionnaires dealing with drug usage, but the advantage is blunted by questionable candor of patients' answers. Use of questionnaires – and, thereby, NARX scores – would be enhanced by questions eliciting more honest answers.
Design and Participants. Our research explores the utility of questions relating to food-addictive behaviors as proxies for and/or adjuncts to standard questionnaires. Our questions' respondents were 100+ chronic pain patients with well-developed patient-profiles, including up-to-date NARX scores. The patients responded to the same areas of inquiry found on standard questionnaires directly probing patients' drug exposure / use / abuse / addiction, but with food categories as selection-choices: Questions regarding what a patient would intake for improvement of mood; in the absence of which, the patient experiences withdrawal; intake of which, diminishes participation in normal activities; etc., were followed by selection-choices of such foods as 'Chocolate' and 'Meat' in place of selection-choices of drugs – with a total of eight questions, each presenting an identical set of four food selection-choices. Our questionnaire elicited over 800 question-selection pairs (*e.g.,* mood-Chocolate; mood-Meat; withdrawal-Chocolate; withdrawal-Meat). Relationships between NARX scores and respondents' choices were assessed by linear regression and t-distribution analyses.

Results. For particular question-selection pairings, the statistical analyses demonstrated strong correlations between risk factors reflected in NARX scores and food-addictive behavioral patterns. Notably, Meat as the selection for those high-correlation questions was associated with the chronic pain patients with the highest NARX scores (*i.e.*, at highest risk); Cheese, the lowest. Other foods reported with high frequency were sodas and sweets, underscoring the role of sugar in chronic pain syndromes.

Conclusions. Questionnaires probing selected food-addictive behaviors, with higher expectation than drug-related questions of eliciting honest answers, may serve to complement patient-profiles with regard to addiction-vulnerability and, thereby, enhance the use of NARX scores in confronting current rising tides of drug addiction, such as those currently manifested in the growing opioid epidemic. We note the utility of such food-centric questionnaires in building addiction profiles in demographics that may not have informative NARX scores, such as recent immigrants. We advocate further clinical studies exploring food-addictive behaviors as proxies for and/or adjuncts to drug-addictive behaviors.

Keywords: addiction; addiction-vulnerability; epidemic; food-addictive behavior; NARX; Opiate Use Disorder; opioids; overdose

INTRODUCTION

Current alarming increases in drug-related deaths in the United States underscore the pressing need for multiple, complementary, readily obtained and reliable indices of a patient's vulnerability to addiction. All fifty U.S. states now electronically share their Prescription Drug Monitoring Program (PDMP) data; this has facilitated the availability to prescriber, pharmacist and law enforcement of a patient's NARX score (as detailed below in section **Technical Background**, the NARX score is a three-digit objective index reflecting a patient's possible intake amounts of narcotics, sedatives and stimulants, and is taken as a predictor of unintentional drug-overdose death [1]). Elevated NARX scores may be indicative of propensities to addiction and may flag the need, at the least, for patient-prescriber discussions regarding drug use and abuse [2]. Intervention may be warranted in cases of high NARX scores.

An up-to-date NARX score may be a particularly meaningful datum when considered in the context of a multi-dimensional patient-profile. Value can be added to such profiles – even those informed by years of trusted patient-prescriber interaction – by patients candidly answering questionnaires regarding their health, including matters of drug use / abuse / addiction. The degree of honesty in patients' answers to the latter questions may be, at best, difficult to assess and, at worst, notably suspect.

We present results of a Comprehensive Pain Management Institute (CPMI) survey questionnaire of our design providing useful adjunct information to that which may be gleaned from standard drug-use questionnaires and may, thus, help to inform patient profiles and enhance the usefulness of NARX scores in such profiles. We believe that our survey, dealing with cravings for food rather than for drugs, carries a realistically high expectation of eliciting honest responses. Analysis of questionnaire data from 110 respondents – CPMI patients with well-developed patient-profiles and up-to-date NARX scores – demonstrates a notable statistical significance of correlation between NARX scores and frequency of answers to particular survey questions regarding select food categories.

Respondents did not report unease in dealing with the questions encountered on the survey questionnaire; some indicated that they enjoyed the questionnaire. The questionnaire is easily administered and suggests itself for wide use. We point, also, to our survey questionnaire as a tool to begin to build addiction profiles in demographics, such as of recent immigrants or young teenagers, which may not have informative PDMP histories.

Background Rationale for Study

A growing body of research is progressively elucidating effects of drug addiction on brain activity of humans and of human-model animals. A representative such research study highlighted the relation between amphetamine and cocaine use on dopamine activity in the brain; the higher the doses of drug consumed, via injection or other routes, the higher the dopamine release activity in the brain's nucleus accumbens (NAc) [3]. The NAc, located in the basal forebrain, with one nucleus in each cerebral hemisphere, is well established as playing a key role in motivational and emotional responses [4]. The NAc is also activated by eating and plays an important role in food addiction [5, 6]. With the same part of the brain activated by drug addiction as by food addiction to provide similar pain-relieving effect [6, 7], recognizing signs of food addiction in its correlation with chronic pain may potentially play an important role in providing insight into high-risk drug-addictive behaviors in chronic pain patients. Our research study was designed to explore, identify and assess relationships between food addiction-related behavior in chronic pain patients and between the effectiveness of NARX score in predicting high-risk factors in such patients.

Relationship between Dopamine and Food Addiction

Dopamine (DA), a monoamine catechol, serves as a neurotransmitter regulating emotional and motivational behavior; it is widely recognized as being associated with reward-related behaviors. The cited research is suggestive of eating behaviors, which are related to the DA reward circuitry of the brain, being measurably comparable to drug addiction, which also involves the DA reward circuitry of the brain [5-7].

In particular, the research indicates that drug addicts and the obese appear to show dysfunction of dopamine D2 brain receptors, with similar – if not identical – brain regions being activated by food-related and by drug-related cues. D2 dopamine auto-receptors are one of five types of DA receptors that have been identified, D1-D5, all of which are transmembrane proteins that play crucial roles in regulation of everyday life functions. D2 receptors are expressed in several brain regions besides the NAc (as well as in some areas outside the nervous system, such as the pulmonary artery and renal glomeruli, conferring upon such areas direct dopamine-sensitivity). The D2 receptors seem to mainly impact functions related to memory, attention, learning, locomotion and sleep [8].

Almost a quarter century ago, a relationship between the level of DA receptors and drug addiction had been presented, whereby low D2 receptor levels were reported as predictive of drug addiction, the drugs used as a means of compensation for decreased activation of the reward circuitry system [9]. Later studies, noted above, demonstrated that amphetamine / cocaine intake increases DA levels in the NAc, which is normally activated by eating, suggestive of NAc release of DA in response to eating being a factor in food addiction [6, 7].

The Effect of Food Addiction on Pain

The cited research went beyond finding generalized correlation between food and chronic pain, expressly identifying foods high in sugar, calories and/or fat as delivering notable pain relief to chronic pain patients. The pain relief is thought to be achieved through interference with endogenous opioid pathways and by reducing activity of brain regions that monitor and/or react to pain [7], specifically by modulation of activity of DA pathways / regions, the same pathways / regions as those implicated in amphetamine and cocaine use.

As promulgated by the Arthritis Foundation [10] and given a firm basis in *Arthritis Research and Therapy*, foods high in sugar, gluten, casein, refined carbohydrates and/or saturated fats evoke an inflammatory response in the body by triggering the release of immune system cytokines [11-14]. Persistent inflammation can eventuate damage of diverse body parts, including skeletal joints. Concomitantly, weight gain usually accompanying disproportionate intake of fatty and/or high caloric foods stresses skeletal joints. Such joint damage may lead to osteoarthritis, with its attendant chronic and progressive pain.

As cited, patients reporting a higher level of pain than others were more inclined to eat foods that were less healthy, with higher levels of fat, calories or sugar [7], thus perpetuating, through the very same foods, a vicious cycle of sought-after pain alleviation and consequent pain persistence.

RESEARCH STUDY

Objective

The purpose of the research study was to explore, identify and assess relationships between food addiction-related behavior in chronic pain patients and between the effectiveness of NARX score in predicting high-risk factors in such chronic pain patients. The study aims to elucidate the roles of dietary factors and food addictions in the development of addictive behaviors and possibly, then, by extension, in the development of the opioid epidemic.

Method

Our cross-sectional study group comprised 110 randomly chosen CPMI chronic pain patients whose histories included having been on opioid medications for more than three months; of ages 40-65 years; with a range of lifestyle- / genetics- / age-related conditions that included hypertension, coronary artery disease, type 2 diabetes mellitus and osteoarthritis. The group's gender distribution was female:male ~ 60:40; the ethnicity distribution was ~ 5% Latino, ~ 35% African American and ~60% Caucasian.

The study group's average NARX score was 383.5 and the median was 380 (highest group score, 740; lowest, 80).

The study group completed an eight-question survey that addressed the following elements of addictive behavior:

- Q1 Consumption to feel better or to change mood
- Q2 Tolerance
- Q3 Withdrawal
- Q4 Consumption of more than initially intended
- Q5 Tried to reduce / stop, but failed
- Q6 Spending substantial time (> 2 hours daily) in recovering from effect or trying to acquire / consume
- Q7 Reduction of normal activities
- Q8 Physical / Mental health problems

The above areas of inquiry are often the topics of questionnaires directly related to drugs, those questionnaires being used to help construct patient-profiles of drug exposure / propensity / vulnerability / use / abuse / addiction. Such questionnaires are often employed upon new-patient intake and have become part of patients' waiting-room activities at annual or other regularly scheduled checkups.

Being built on the template of those widely accepted and frequently employed addiction-evaluation questionnaires, our survey questionnaire is expected to have at least commensurate validity / applicability. Our questionnaire has shifted the focus of the questions from drugs to food-types, providing questions that – while deemed less intrusive / threatening than the same questions typically focused on drugs – were designed to reveal information pertaining to food-addictive behaviors that might be applicable to drug-addictive behaviors.

The same set of four available selection-choice answers was presented below each of eight questions:

a. Chocolate b. Cheese c. Meat d. Other

(with space provided for voluntary respondent-identification of 'Other')

The eight questions of the research survey questionnaire were:

Q1. Which of the following foods have you ever had persistent desire for or take more than once to feel better or to change your mood?

Q2. Which of the following foods have you needed to increase the amount of to get the same effect that you did when you first started taking it?

Q3. Reduction or discontinuation of which of the following foods caused you withdrawal symptoms (aches, shaking, fever, weakness, diarrhea, nausea, sweating, heart pounding or difficulty sleeping; or feeling agitated, anxious, irritable or depressed)?

Q4. Which of the following you ended up taking more than you thought you would?

Q5. Which of the following have you tried to reduce or stop eating, but failed?

Q6. On the days you have eaten the following foods, did you spend substantial time (> 2 hours) in trying to get them, eat them, recover from their effects, or thinking about them?

Q7. Which of the following have you ever reduced your activities (e.g., hobbies, work, daily activities) for or caused you to spend less time with your family or friends?

Q8. Which of the following foods do you continue to consume even though they cause health or mental problems?

Results

Questionnaire Responses

While respondents were not limited to selecting only one answer-choice per question, the vast majority of questions received only one answer per respondent. Some respondents left one or more questions unanswered.

Response frequencies to the study survey questions are given in Table 1.

TABLE 1: RESPONSE FREQUENCY BY QUESTION AND ANSWER					
	Chocolate	Cheese	Meat	Other	Totals (by question)
Q1 Mood	**33**	**16**	**15**	**46**	110
Q2 Same Effect	**12**	**9**	**20**	**61**	102
Q3 Withdrawal	**10**	**7**	**10**	**74**	101
Q4 More Than Thought	**22**	**9**	**18**	**56**	105
Q5 Reduce / Stop But Fail	**18**	**10**	**16**	**57**	101
Q6 Recover from Effect	**9**	**6**	**10**	**75**	100
Q7 Reduce Activities	**11**	**2**	**11**	**74**	98
Q8 Health / Mental Problems	**22**	**3**	**9**	**67**	101
Totals (by answer)	137	62	109	510	**818**

Table 1 background / comments: From the 110 patients who completed the form, 880 answers (8 questions times 110 respondents) would be the expected total number of responses. However, the survey generated 818 answers (see Table 1; bottom-right data cell), as some patients did not respond to all eight of the questions, leaving one or more of the questions unanswered / blank. When a question was not answered, the survey was still counted, but the specific unanswered question was entered as 'missing,' without a numerical effect on the total non-blank response frequency for that question. Additionally, as noted, some few questions received more than one answer from a given respondent.

Of the possible answers, 'Other' was most often selected, with a total of 510 responses, and 'Chocolate' was the second most often selected, with a total of 137 responses. Of the 510 'Other' responses, 423 of those answers were given as 'None' or 'NA' or left blank. When foods were identified under 'Other', there were 39 occurrences of 'Coffee'; 23 of 'Pepsi', 'Soda' or 'Mountain Dew'; and 12 each for 'Bread(s)' and 'Sweets'.

NARX Scores

Average NARX score of respondent-cohorts by question and answer are given in Table 2.

TABLE 2: AVERAGE NARX SCORE BY QUESTION AND ANSWER				
	Chocolate	Cheese	Meat	Other
Q1 Mood	**376.7**	**293.8**	**391.3**	**401.5**
Q2 Same Effect	**340.8**	**358.9**	**438.0**	**377.0**
Q3 Withdrawal	**376.0**	**412.9**	**373.0**	**385.9**
Q4 More Than Thought	**379.5**	**312.2**	**423.9**	**383.9**
Q5 Reduce / Stop But Fail	**401.1**	**395.0**	**422,5**	**371.8**
Q6 Recover from Effect	**341.1**	**375.0**	**424.0**	**385.2**
Q7 Reduce Activities	**335.5**	**405.0**	**358.2**	**390.8**
Q8 Health / Mental Problems	**403.6**	**390.0**	**388.9**	**377.3**

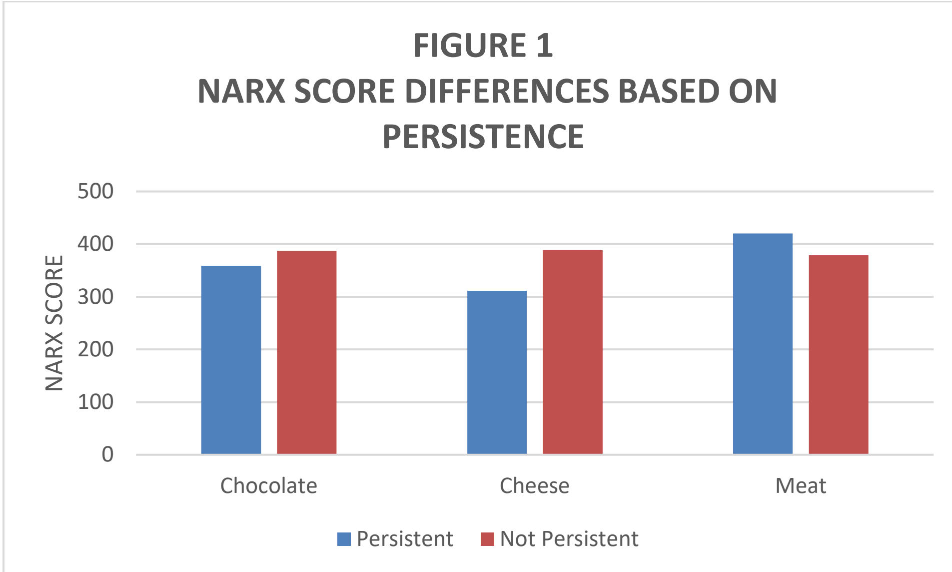
Table 2 background / comments: The average NARX scores of respondent-cohorts is given for each question-answer pairing. Thus, for example, the value of 376.7 reported in the upper-left data cell of the table is the average NARX score of the 33 respondents that answered 'Chocolate' to Question 1. (The values reported in the 'Other' column are averages over the scores of all group members answering 'Other' to a given question, irrespective of those members providing voluntary respondent-identification of 'Other' or leaving it unidentified.) The cells highlighted in orange contain the four highest respondent-cohort average NARX scores and the cells highlighted in blue contain the four lowest respondent-cohort average NARX scores. Of possible interest is the fact that the four highest average NARX scores are associated with eating meat. The two lowest average NARX scores are associated with eating cheese.

Before considering our linear regression statistical analyses (for details of which, see section **Correlations of Questionnaire Responses with NARX Scores** and section **Technical Background**, both below) and the significance of correlations between NARX scores and questionnaire responses brought to light by the analyses, we present explorations of trustworthiness of and trends within the data. Such explorations will help define the scope of investigation carried out on the data.

For instance, from a cursory examination of Table 1, it is difficult to assess whether the fall-off from Q1's high total response-tally, 110, to the lower tallies of the subsequent questions is a function of a precipitous post-primacy drop in enthusiasm for answering questions after having encountered and answered the first; is a function of the nature / contents of the questions; lies in some middle-ground between those two possible explanations; and/or lies with some other factor(s). That Q4's total response-tally, 105, has crept up close to that of Q1 from those of the intervening questions, might indicate that, even if a post-primacy drop is operative, the contents / nature of the questions is a factor at play in the response-tallies. Thus, Q7's lowest total response-tally may reflect not just waning enthusiasm for answering the questionnaire (followed by a slight finish-line rallying), but may also indicate an element of guilt / shame engendered by consideration of the negative effect of the food-craving on normal life / social functioning focused on by Q7. Without objective statistical analyses of the data, such suggestive, but not compelling, interpretations abound. In this instance, it is important to realize that the response-tallies vary by less than 8% from their average value of ~102.3 and that, therefore, conjectures as to any meaning to the differences in response-tallies may be statistically unfounded.

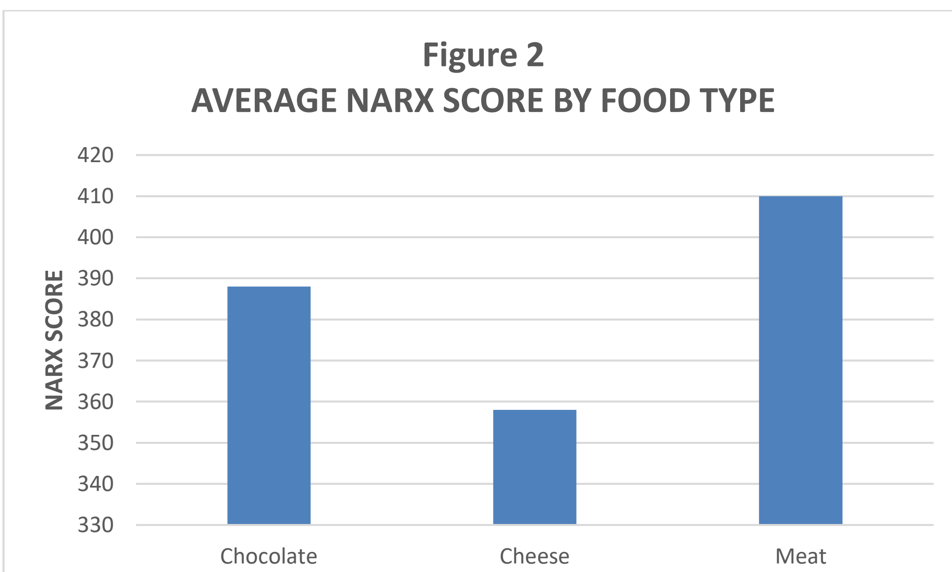
Many respondents gave the same answer to multiple questions. There were 33 respondents (30% of the study group) that gave the same answer to all eight questions; in most of those cases, that answer was 'Other'. We label as "persistent" those patients who responded with the same choice to four or more of the eight questions. Persistent respondents may have rushed though the survey and/or may have been careless / dismissive of half or more of the eight questions, giving little thought to those questions and, therefore, giving the same response as a short-cut, rendering their answers uninformative. On the other hand, a respondent's persistent use of the same choice – even for all eight questions – may have been a matter of deliberate intentionality following due consideration of each question, weighing the choices as they pertain to that question and then selecting the appropriate honest and properly informative answer.

Assuming that the rushing / careless / dismissive interpretation of persistence of the persistent respondents is reflective of behavior profiles different from those of non-persistent respondents, one might expect to see marked differences per choice in average NARX scores between the persistent and the non-persistent. The bar graph of Figure 1 demonstrates, however, that there is no statistically significant distinction between persistent respondents and non-persistent respondents reflected in their average NARX scores, with only minor and trend-less differences appearing. (Cheese alone demonstrates a difference greater that 10% from the average in the persistent and non-persistent NARX scores, but still less than 15%. More sophisticated statistical methods bear out the premise of a lack of significance of food-type persistence, with the possible exception of Cheese.) The implication is that answers of persistent respondents are not less trustworthy than those of non-persistent respondents as indicators of the deliberate, informative choices of response to the questions.



Another check of factors that may have influenced choice-frequency independent of respondents' consideration of selecting the appropriate answer to a given question, involves the attractiveness / appeal of one or the other of the food-choices regardless of the particulars of the question. It could be that 'Chocolate' or 'Cheese' or 'Meat' would be the selection of choice to "Of the following, what is your favorite food? / …has the most enticing odor? / …reminds you of fond childhood memories? / …would you choose as the color of your next car? / etc."

The bar graph, with expanded vertical scale, of Figure 2 demonstrates, however, that there are only minor differences in NARX scores based on Food Type. The only food-type pair with a NARX score difference that exceeds a simple coarse measure of significance, ~10% of the pair's average, is the difference between Cheese and Meat and thus, may, indeed, account in a minor fashion for trends in our data.



Yet another factor, sequence-placement of each selection-choice, seems not to have been at play. For a given question, respondent-totals per selection-choice (see Table 1) show no trends other than a bunching up at last-placed 'Other', which latter is readily accounted for by 'Other' simply being the only option to choose when none of the more specific choices was apt.

<u>Correlations of Questionnaire Responses with NARX Scores</u>

Multiple linear regression processing and results

Multiple linear regression analysis was performed on the 100 respondents' data-sets, giving a "least-squares" best fit of the data to the equation

$$\mathbf{NARX} = \sum_{i=a}^{d} \sum_{j=1}^{8} \mathbf{Qi{:}j\ Xi{:}j} + \mathbf{c}\text{onstant},$$

terms of which are defined as:

for each selection-choice **i** (i = a, b, c, d)
of each survey question **j** (j = 1, 2,…8),
each of the 32 question-selection pairs **Qi:j**
(e.g., **Q1:b** ≡ question **1** [Mood]: selection-choice **b** [Cheese])

serves as a coefficient multiplying a respondent-specific datum, **Xi:j,**

of a respondent <u>selecting</u> (**Xi:j = 1**) or
<u>not selecting</u> (**Xi:j = 0**)
selection-choice **i** for question **j.**

(For more information regarding the equation and processing, see section **Technical Background** below; for linear regression primer/refresher, see, e.g., [15, 16].) The resulting 32-term equation was assigned an initial set of **Qi:j** values and then evaluated for each of the 110 respondent-specific data-sets of **Xi:j**'s, with the difference between the respondent's equation-estimated NARX score and the respondent's known NARX score squared (giving a positive measure of the difference, the actual difference as likely to be negative as positive) and the 110 squares summed. Following standard linear regression analysis steps, **A**] **Qi:j**'s were then adjusted; **B**] the new 32-term equation was evaluated for each of the 110 respondent-specific data-sets of **Xi:j**'s; **C**] squares of the 110 differences of equation-estimated NARX scores from known NARX scores were summed; and **D**] the new sum was compared to the previous such sum of squares. **A**] - **D**] were iteratively stepped through until achievement of the minimum ("least") sum of the squares, giving 32 "best-fit" **Qi:j** values for the equation. Each best-fit **Qi:j** can be thought of as the slope of the NARX score along the **i:j**-axis (there being 32 axes in the 33-dimensional space under consideration in this multiple linear regression model, the y-axis being NARX score), providing a measure of the correlation of each **i:j** question:selection pair with the NARX score.

We present in Table 3 the probabilities of chance alone accounting for the value of the regression analysis best-fit **Qi:j** coefficients for correlation between an i:j question:selection pair and NARX score (see **Appendix**, below **References**, for the 32 best-fit Qi:j coefficients tabulated with their associated, and briefly defined, standard errors, t-values and probabilities). The lower the probability of being by chance, the higher the likelihood of a given question:selection pair **Qi:j** being significant; i.e., the lower the presented probability, the stronger the correlation of the question:selection pair's cohort's NARX values with the question's selection-choice. The Table shows the highest significance of correlations between the food groups and NARX scores coming from question 5 (tried to reduce / stop eating food, but failed) and question 7 (reduce other activities and/or social / family time for the food). (We note that question 7 had the lowest respondent rate, only 98 out of 110 patients, with **Q7:Cheese** exhibiting the lowest of the 32 response frequencies; see Table 1.) Those questions exhibit significance values better than the .05 level for all selection-choices and, for the particular selection-choice of Meat, even better than the .01 level. Thus, in terms of trying to predict NARX scores based on answers to the survey questions, questions 5 and 7 are deemed the most useful, with those questions' Meat selections perhaps deserving special attention.

Statistics also provides a measure of the extent of such usefulness with respect to how thoroughly the regression analysis' **Qi:j** coefficients for the question:selection pairs – both for all eight questions and for the subset of questions 5 and 7 considered apart from the rest of the questions – account for the NARX scores. The measure is given by the statistic termed "R-squared," the coefficient of determination, which may be expressed as a percentage between 0% and 100%. R-squared quantifies how much of the variability of a process has been explained solely by the model's presumed independent factor; i.e., how fully that independent factor predicts the results. Even a high correlation of dependent factor with independent factor does not speak to *how completely* that independent factor accounts for the dependent factor results. As an illustrative example, the R-squared value for the relationship between ice cream sales (the dependent factor in this food-related model illustration) and temperature (the independent factor) would be expected to be quite close to, but realistically still less than, 100% after full analysis of data by linear regression. One would, on that basis, conclude that temperature is a very good predictor (or determinant) of ice cream sales, without a need to consider other factors playing major roles. On the other hand, the R-squared value for the relationship between ice cream sales and downloads of Beethoven's Fifth Symphony would be expected to have a low R-squared value, likely quite close to but not necessarily 0%, and Beethoven's Fifth would not be considered a good predictor of ice cream sales. Models' R-squared values above 0% and below 100% indicate a partial predictive power of a model's independent variable to forecast the dependent variable values, with increase in the predictive power reflected in increasing R-squared value of the model.

The model used to identify which of the survey question-selections correlated most significantly with NARX score, a model taking into account respondent data of all eight questions, exhibited an R-squared value of 35%. A more focused model measuring the relationship between NARX score and data of only questions 5 and 7, exhibited an R-squared value of 16%. These sub-50% R-squared values suggest that foods are important predictors (or determinants) of NARX score – with some questions:selection pairs being particularly trustworthy forecasters – but that there are other factors, as yet unidentified, that individually or collectively play larger roles.

TABLE 3: PROBABILITY OF SIGNIFICANCE
Green background: Significance at better than the .01 level
Blue background: Significance at better than the .05 level, but not .01

	Chocolate	Cheese	Meat	Other
Q1 Mood	0.529	0.034	0.496	0.598
Q2 Same Effect	0.824	0.505	0.247	0.752
Q3 Withdrawal	0.880	0.855	0.314	0.603
Q4 More than Thought	0.943	0.754	0.944	0.777
Q5 Reduce / Stop but Fail	0.010	0.017	0.006	0.025
Q6 Recover from Effect	0.965	0.602	0.925	0.460
Q7 Reduce Activities	0.014	0.047	0.005	0.025
Q8 Health / Mental Problems	0.931	0.750	0.709	0.609

Technical Background
NARX Score

The NARX score is a U.S. patient-assessment tool calculating usage amounts of narcotics (opioids), sedatives, and stimulants [1, 2, 17]. The NARX score, widely employed in the U.S., uses a particular calculation system set to three digits, with a range from 000 to 999. The score corresponds to a number of literature-based risk factors that exist within the patient's PDMP data [1, 2, 17]:
a. The number of prescribers providing prescriptions to the patient
b. The number of pharmacies filling the patient's prescriptions
c. The amount of medication dispensed (often measured in milligram equivalencies) to the patient
d. The number of times the patient's prescriptions of a similar type overlap from different prescribers

NARX scores for patients of a typical PDMP distribute approximately as: 75% score less than 200; 5% score more than 500; 1% score more than 650 [17]. NAXR scores were designed such that patients who use small amounts of medication with limited provider and pharmacy usage will have low scores, and vice versa. The NARX score is considered an effective reference to patients in the pain management area [1] and is considered to provide actionable data [2].

Statistical Analysis

The equation evaluated for each of the 110 respondents is given in Figure 3.

FIGURE 3
Equation

$$NARX_{estimate} = \sum_{i=a}^{d} \sum_{j=1}^{8} Qi{:}j\ Xi{:}j =$$

$$Q_{1:a}X_{1:a} + Q_{1:b}X_{1:b} + Q_{1:c}X_{1:c} + Q_{1:d}X_{1:d} +$$

$$Q_{2:a}X_{2:a} + Q_{2:b}X_{2:b} + Q_{2:c}X_{2:c} + Q_{2:d}X_{2:d} +$$

$$Q_{3:a}X_{3:a} + Q_{3:b}X_{3:b} + Q_{3:c}X_{3:c} + Q_{3:d}X_{3:d} +$$

$$Q_{4:a}X_{4:a} + Q_{4:b}X_{4:b} + Q_{4:c}X_{4:c} + Q_{4:d}X_{4:d} +$$

$$Q_{5:a}X_{5:a} + Q_{5:b}X_{5:b} + Q_{5:c}X_{5:c} + Q_{5:d}X_{5:d} +$$

$$Q_{6:a}X_{6:a} + Q_{6:b}X_{6:b} + Q_{6:c}X_{6:c} + Q_{6:d}X_{6:d} +$$

$$Q_{7:a}X_{7:a} + Q_{7:b}X_{7:b} + Q_{7:c}X_{7:c} + Q_{7:d}X_{7:d} +$$

$$Q_{8:a}X_{8:a} + Q_{8:b}X_{8:b} + Q_{8:c}X_{8:c} + Q_{8:d}X_{8:d}$$

with **Xi:j**, for question **i**, for a given respondent, being either **1** (if respondent selected choice **j**) or **0** (if respondent did **not** select choice **j**)*

* For a given respondent and a given question **i**, three out of four of the Xi:j were, typically, zero (0), thus multiplying by zero the corresponding **Qi:j**'s. But, over the group of 110 respondents, each of the individual **Qi:j**, for any given **i** and **j**, does occur multiplied by 1; i.e., all selection-choices for specific food-types choices a-b-c were chosen at least once for each question by the group as a whole, as seen above in Table 1, where the frequency of a-b-c selection ranges from 2 to 33. (As noted, the non-specific choice d, 'Other', enjoyed the highest group response frequency for all questions.)

The public-domain regression program **R** was employed to achieve the least-squares best-fit set of the 32 **Qi:j**'s in 33-space, with NARX as the y-axis and 32-non-y-axes, each **Qi:j** interpretable as the slope of NARX value along the **i:j** axis, the slopes sharing a common NARX value y-axis intercept. In the course of the iterations, the **Qi:j** values were adjusted with an aim of lessening the sum of the squares of the differences of equation-estimated NARX scores from known NARX scores; and the adjusted equation was evaluated anew for each of the unchanging 110 respondent-specific data-sets of **Xi:j**'s; squares of the 110 differences between $NARX_{equation}$ and $NARX_{known}$ were summed; and the new sum was compared to the previous such sum of squares, until the sum of the squares of the differences was brought to an absolute minimum (achieving a "least-squares" solution), giving 32 "best-fit" **Qi:j** values for the equation.

Each of the 32 **Qi:j** linear **slopes** thus arrived at is characterized by a standard error, $\mathbf{SE_{i:j}}$ (roughly, the average of the displacement of the **i:j** data points from the best-fit line; see e.g., [18-20] for straightforward presentations of terms and definitions) and was analyzed to provide a t-value given by $\mathbf{slope_{i:j}/SE_{i:j}}$. A standard t-distribution table yields the associated probability $\mathbf{p_{i:j}}$ of significance. (See **Appendix** Table for all values.)

DISCUSSION

With the alarming explosion of overdose risk evidenced in the opioid epidemic since the late 1990s, Opiate Use Disorder (OUD) in the U.S. has cost tens of thousands of lives, estimated at the time of this writing (early 2023) at over 900,000 [21], and is now exacting an annual economic toll in excess of a trillion $USD [22, 23].

Early waves of the epidemic — a first wave having started by about 1999 when overdose deaths from prescription opioids, several then newly FDA-approved for pain alleviation, exceeded those from heroin; and a second wave, from about 2010, marked by a notable resurgence of heroin deaths — have been dwarfed by the current third wave of rising U.S. drug-overdose deaths, at least 70% opioid-related. The third wave is considered to have started a decade ago, by 2013, when powerful fully synthetic opioids such as earlier-developed fentanyl and tramadol began to widely penetrate the prescription and illicit markets [24].

Starting around 2016, the third wave saw a dramatic steepening of its rise as overdose deaths from fully synthetic opioids outpaced the then leveling-off / down-trending death-count of roughly 13,000 nationwide (4 per 100,000 population-count) for each of heroin and of more routinely prescribed pain medication such as methadone and natural and semi-synthetic opioids. By 2019, U.S. annual opioid overdose deaths had reached approximately 50,000 (16 per 100,000 population-count), with almost three quarters of that toll directly attributable to the powerful fully synthetic opioids [24]. The rapidly worsening opioid crisis, while perhaps most severe (and/or perhaps most thoroughly reported) in the United States, is of global impact, accounting by WHO statistics for about 70% of 2019's estimated half-million global drug overdose deaths [25].

The highly perturbing 2019 U.S. numbers now seem tame in view of the escalating drug-related fallout from severe psycho-social effects of 2020-2021's local, state and federal SARS-Cov-2 responses, coupled with a soaring supply of illicit drugs (of particular concern, fentanyl-laced drugs), at least partly via increasingly rampant drug smuggling across the U.S. southern border [26, 27]. For the twelve-month period ending in April, estimates of U.S. drug fatalities in 2020 put opioid-related overdoses at about 56,000 out of an overall overdose death toll of about 78,000; and, in 2021, at about 75,700 opioid-related overdoses out of an overall overdose death toll of about 100,000 [28].

With a focus now on Ohio, where our study was conducted, research conducted in 2017 on opioid mortality showed Ohio (OH) to have the second-highest opioid mortality rate in the U.S., with more than 2.6 times the death rate per 100,000 population-count compared to the U.S. average, at 39.2 in OH vs. 14.6 in U.S. Since 2017, OH overdose mortality has increased annually (except for a single one-year interval), reaching more than 5,500 deaths in 2021 (from May 2020 to April 2021), a 26.6 percent increase over the previous year [29, 30]. Just Ohio's Franklin County, home to our Columbus-based study, alone lost more than 3,500 people from 2018 to 2022 from drug overdoses, based on county coroner's data [31].

In addition to its huge death toll and direct economic costs, OUD has had and continues to have significant secondary impacts at numerous societal levels, many of those impacts likely to have repercussions for decades to come: Disruption of family structure; fracturing of formative years of children born to and/or raised in distressed families; under-the-influence substance-related motor vehicle accidents; rampant crime, including violent crime, and the consequent "normalization" of all varieties of crime; et al. By way of illustration, in June 2022, every branch of the U.S. military, a non-conscription / all-volunteer force, reported struggling to meet annual recruiting goals; drug use and criminal records, the latter often tied to drugs, disqualified the majority of potential recruits, with only 23% of applicants qualifying [32].

Even the possibility that some of the local, national and global OUD deaths could have been prevented by early access to addicts' dietary data, underscores the pressing need for further study of the roles of diet / lifestyle information and modification in addictive behavior.

CONCLUSION

There is a strong correlation between high-risk factors in chronic pain patients as manifested and measured by the NARX score and between food addictive behavioral patterns in those chronic pain patients. Of the three food-categories (selected with an eye to earlier research [33]) explicitly surveyed in the study questionnaire — chocolate, cheese, meat — meat was associated with the highest NARX scores in chronic pain patients, *i.e.*, with the highest risk chronic pain patients; cheese, with the lowest. Chocolate was reported most often of the three; non-explicitly surveyed foods reported with high frequency were coffee, sodas and sweets, underscoring the role of sugar in chronic pain syndromes.

Questionnaires probing selected food-addictive behaviors may serve to complement patient-profiles with regard to addiction-vulnerability. Food-related questions carry a higher expectation than drug-related questions of eliciting honest answers. The food-related questionnaires may enhance the use of NARX scores in confronting current rising tides of drug addiction.

The more information available and the more readily and earlier such information may be available about individuals' propensities to addiction, the more that can be done to stem the tide of addiction's ravages. While a complex web of socio-economic factors may be driving OUD's broadening and deepening severity, our research suggests that food addiction may play a significant role in the crisis, presenting a modifiable factor that should be evaluated, addressed and judiciously utilized by prescribers, pharmacists, law enforcement (including, potentially, use of prison diets as an indirect form of intervention), educators and parents.

We advocate further clinical studies exploring food-addictive behaviors as proxies for and/or adjuncts to current measures of drug-addictive behaviors and, more generally, on the topic of food addictive behavioral patterns in chronic pain patients and in lifestyle modifications.

Ethics Statement

The Comprehensive Pain Management Institute (CPMI) is a small independent practice. We confirm that the CPMI ethics board approved this study. All participants gave consent. No PHI was exposed.

References

1. Huizenga J.E., Breneman B.C., Patel V.R., et al. (2016) NARxCHECK® Score as a Predictor of Unintentional Overdose Death. Appriss, Inc.

2. Cochran G., Brown J., Yu Z., et al. (2021) Validation and threshold identification of a prescription drug monitoring program clinical opioid risk metric with the WHO alcohol, smoking, and substance involvement screening test. *Drug Alcohol Depend.* 228: 109067. PMID: 34610516

3. Volkow N.D., Tomasi D., Wang G-J., et al. (2014) Stimulant-induced dopamine increases are markedly blunted in active cocaine abusers. *Mol Psychiatry* 19 1037-1043. DOI: 10.1038/mp.2014.58. PMID: 24912491

4. Fernández-Espejo E. (2000) Cómo funciona el nucleus accumbens? [How does the nucleus accumbens function?]. *Rev Neurol.* 30(9):845-9. Spanish. PMID: 10870199

5. Kelley A.E. (2004) Ventral striatal control of appetitive motivation: role in ingestive behavior and reward-related learning. *Neurosci Biobehav Rev.* 27(8):765-76. PMID: 15019426.

6. Baik J-H. (2013) Dopamine signaling in food addiction: role of dopamine D2 receptors. *BMB Rep.* 46: 519-526. DOI: 10.5483/BMBRep.2013.46.11.207 PMID: 24238362

7. Choi K.W., Somers T.J., Babyak M.A., et al. (2014) The relationship between pain and eating among overweight and obese individuals with osteoarthritis: An ecological momentary study. *Pain Res Manag* 19: e159-e163. DOI: 10.1155/2014/598382

8. Mishra A., Singh S., Shukla S. (2018) Physiological and Functional Basis of Dopamine Receptors and Their Role in Neurogenesis: Possible Implication for Parkinson's disease. *J Exp Neurosci.* 12:1179069518779829. DOI: 10.1177/1179069518779829. PMID: 29899667

9. Volkow N.D., Wang G-J., Fowler J.S., et al. (1999) Prediction of reinforcing responses to psychostimulants in humans by brain dopamine D2 receptor levels. *Am J Psychiatry* 156: 1440-1443. DOI: 10.1176/ajp.156.9.1440

10. Arthritis Foundation (2019) Arthritis Diet.

11. Lee K.MC., Zhang Z., Achuthan, A., et al. (2020) IL-23 in arthritic and inflammatory pain development in mice. *Arthritis Res Ther* 22, 123. DOI: 10.1186/s13075-020-02212-0

12. Vedder D., Gerritsen M., Duvvuri B, et al. (2020) Neutrophil activation identifies patients with active polyarticular gout. *Ibid.,* 148. DOI: 10.1186/s13075-020-02244-6

13. Liu Q., Hebert J.R., Shivappa N., et al. (2020) Inflammatory potential of diet and risk of incident knee osteoarthritis: a prospective cohort study. *Ibid.,* 209. DOI: 10.1186/s13075-020-02302-z

14. Wu Y., He X., Huang N, et al. (2020) A20: a master regulator of arthritis. *Ibid.,* 220. DOI: 10.1186/s13075-020-02281-1

15. https://towardsdatascience.com/linear-regression-explained-1b36f97b7572

16. https://www.scribbr.com/statistics/multiple-linear-regression/

17. State of Ohio Board of Pharmacy (2019) Ohio Automated RX Reporting System (https://ohiopmp.gov)

18. *https://www.statology.org/standard-error-regression*

19. *https://www.statology.org/t-test-linear-regression*

20. *https://www.scribbr.com/statistics/* t-distribution/

21. https://www.cdc.gov/drugoverdose/deaths (accessed Sep. 21, 2022)

22. Florence C., Luo F., Rice K. (2020) The economic burden of opioid use disorder and fatal opioid overdose in the United States, 2017. *Drug and Alcohol Dependence* 218:108350. DOI: 10.1016/j.drugalcdep.2020.108350 PMID: 33121867

23. Jennings K. (2022) Economic Toll of Opioid Epidemic: $1.3 Trillion A Year Forbes Feb. 4, 2022

24. *https://www.cdc.gov/opioids/basics/epidemic.html*

25. https://www.who.int/news-room/fact-sheets/detail/opioid-overdose (accessed Sep. 21, 2022)

26. *https://www.gov/washington/testimony/2022/t20220726.htm.*

27. *https://www.cnn.com/2022/01/08/us/fentanyl-seized-south-texas-border-2021*

28. *https://www.nytimes.com/2021/11/17/health/drug-* overdoses-fentanyl-deaths.html

29. Boggs J. (2021) Ohio drug overdose deaths jumped 26% in a year. *Spectrum News 1* Dec. 8, 2021 (https://www.notfarfromme.org/news/ohio-drug-overdose-deaths-jumped-26-in-a-year)

30. Nissen N. (2021) Opioid overdoses 29% higher in 2020 than before the pandemic: Study https://abcnews.go.com/Health/opioidoverdoses-29-higher-2020 pandemicsstudy/ story?id=75785104

31. Shuda, N. (2023) Five things to know about Franklin County's 2022 drug overdose death numbers. *The Columbus Dispatch* April 21, 2023

32. Kube C. and Boigon M. (2022) Every branch of the military is struggling to make its 2022 recruiting goals, officials say. *NBC News* June 27, 2022

33. Janke E.A., Kozak A. (2012) "The more pain I have, the more I want to eat": obesity in the context of chronic pain. *Obesity* (Silver Spring) 20: 2027-2034. DOI: 10.1038/oby.2012.39

APPENDIX

SUMMARY OF LINEAR REGRESSION OF NARX SCORES VERSUS FOOD TYPE

The following table presents a more in-depth report of the linear regression analysis results described above in text.

Left column **Q1-Q8** refer to questionnaire question numbers 1-8; **a-d** refer to the questionnaire answer selection-choices.

Estimate: value of the least-squares best-fit Qi:j coefficient (**slope** along the i:j axis) estimated by the regression analysis.

Standard Error (SE): confidence interval around **Estimate** (**SEi:j** , roughly the average of displacement of the **i:j** data points from the best-fit line of NARX values vs i:j-axis values).

t-value: (given by (**$slope_{i:j}$ - 0)/$SE_{i:j}$** , where 0 is the null-hypothesis slope value of no dependence of NARX on the particular i:j question:selection pair) used to assess the significance of the **Estimate**; generally, -2>**t-value**>+2 indicates low probability of **Estimate** being accounted for by chance.

p value: (from standard t-distribution table) measure of probability of significance

Full 8-Question model R^2 =35% F=1.205	**Estimate**	**Standard Error**	**t-value**	**p value**	Significant ** at better than .01 level * at better than .05 level
(Intercept)	**360.129**	**105.055**	**3.428**	**0.00102**	**
Q1a	-59.304	93.812	-0.632	0.52932	
Q1b	-198.086	91.398	-2.167	0.03357	*
Q1c	-63.313	92.613	-0.684	0.49643	
Q1d	-52.755	99.622	-0.53	0.59808	
Q2a	29.488	132.368	0.223	0.82435	
Q2b	86.444	129.1	0.67	0.50529	
Q2c	111.684	95.759	1.166	0.2474	
Q2d	32.217	101.516	0.317	0.7519	
Q3a	14.431	95.533	0.151	0.88036	
Q3b	13.08	71.143	0.184	0.85465	
Q3c	84.586	83.44	1.014	0.31415	
Q3d	35.275	67.588	0.522	0.60336	
Q4a	-8.391	117.659	-0.071	0.94335	
Q4b	-30.9	98.077	-0.315	0.75364	
Q4c	7.639	108.099	0.071	0.94386	
Q4d	-31.265	110.165	-0.284	0.77739	
Q5a	296.311	112.356	2.637	0.01026	*
Q5b	282.275	115.603	2.442	0.01711	*
Q5c	348.441	122.571	2.843	0.00584	**
Q5d	251.738	109.892	2.291	0.02495	*
Q6a	5.028	113.111	0.044	0.96467	
Q6b	53.812	102.715	0.524	0.60198	
Q6c	9.055	96.193	0.094	0.92527	
Q6d	72.359	97.413	0.743	0.46005	
Q7a	-305.354	121.049	-2.523	0.01389	*
Q7b	-309.903	153.538	-2.018	0.04733	*
Q7c	-383.653	132.757	-2.89	0.00511	**
Q7d	-258.933	113.234	-2.287	0.0252	*

Q8a	6.365	73.301	0.087	0.93105	
Q8b	39.294	122.925	0.32	0.75016	
Q8c	-32.306	86.212	-0.375	0.70898	
Q8d	-37.636	73.289	-0.514	0.60918	