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Opioid and Alcohol Misuse in Veterans with Chronic Pain: A Risk Screening Study

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Abstract: **In United States military veterans, chronic pain represents a risk factor for opioid and alcohol misuse, yet few studies have examined interactions among chronic pain, opioid prescription, and opioid and alcohol misuse. Previous work found substantial risk of co-morbid alcohol and opioid misuse in a community sample of opioid-prescribed individuals with chronic pain, a finding expanded upon here. Specifically, 211 veterans assessed within a chronic pain treatment service for opioid-prescribed individuals completed self-report measures of opioid misuse, alcohol misuse, pain intensity, depression, pain catastrophizing, and post-traumatic stress symptoms (PTS). Based on the substance misuse measures, 32% (n = 68) were misusing neither opioids nor alcohol, 23% (n = 48) were misusing both opioids and alcohol, 40% (n = 84) were misusing opioids alone, and 5% (n = 11) were misusing alcohol alone. Group comparisons indicated that individuals not misusing either substance were less distressed in comparison to those who were misusing opioids alone or both substances. The latter groups differed in PTS. Overall, misuse frequencies mirrored previous work, with approximately 1 of 3 misusing opioids and approximately 1 of 5 misusing both substances. There is a need for increased focus on both polysubstance misuse and the development of integrated treatment.**

Perspective: ***Opioid and alcohol misuse was examined in 211 Veterans prescribed opioids for chronic pain. In total, 32% were not misusing either, 23% were misusing both, 40% were misusing opioids, and 5% were misusing alcohol. Veterans not misusing either were generally less disabled and distressed compared to those misusing opioids or both.***

Key Words: *Chronic pain: opioids: alcohol: veterans: risk screening.*

Introduction

Chronic pain is one of the most common reasons for treatment seeking among veterans within the United States (US) Veterans Health Administration (VA), with up to 68% experiencing a chronic pain condition.[24,29,34,73] A sizeable proportion of Veterans are prescribed opioids for the treatment of chronic pain. While prescription rates have decreased from their peak in the early 2010's, recent estimates indicate up to one-third have an active prescription.[27,41,43,53] While there is supportive evidence that opioids can reduce pain intensity in those with chronic pain, there is also risk in the form of increased morbidity and mortality.[36,50] Veterans may be especially vulnerable to these risks as the increased use of opioid medications for chronic pain management in this population has been associated with a high risk of co-morbid substance misuse and substance use disorders, polypharmacy (eg, concurrent prescription or use of sedative, hypnotic, or other central nervous system depressant medications), and opioid related overdose deaths.[15,54,87] In veterans, a chronic pain diagnosis doubles the risk of having a

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substance use disorder diagnosis, while an opioid prescription is an independent predictor of the occurrence of a serious adverse event.[6,66] Thus, there is significant interest in the identification of opioid misuse, broadly defined as opioid use contrary to prescribed instructions and/or use that has the potential for harm.

In addition to the risk of opioid misuse, people with chronic pain are also at an increased risk of alcohol misuse.[17,20,38] Alcohol misuse is highly prevalent across the world and represents a significant contributor to morbidity and mortality.[8,40,60,64,67,71,75] Opioid and alcohol co-use ranges from 12% to 36% in the published literature.[12,13,21,22] Further, as both substances are central nervous system depressants, they can have a synergistic interactive effect substantially increasing the risk of overdose (see [85] for a review). This risk has led to clinical guidelines indicating that the prescription of opioid medications is contraindicated for individuals who misuse alcohol [eg, Food and Drug Administration,[19] the Centers for Disease Control and Prevention,[16] and the Veterans Affairs/Department of Defense (VA/DoD, 2017)[74]].

Despite the potential for the misuse of alcohol alone or in combination with opioid misuse, few studies have examined comorbid misuse in those with chronic pain who are prescribed opioids. Several studies have separately evaluated problematic opioid use and alcohol misuse in chronic pain populations.[20,44,52,72,83] However, to our knowledge, only 2 studies have examined alcohol and opioid misuse concurrently in opioid prescribed individuals with chronic pain. The first indicated that "risky drinking", defined as 5 or more drinks on a single occasion, was associated with greater interference from chronic pain.[38] The second included 131 opioid prescribed community-dwelling individuals with chronic pain, who completed screening measures for opioid and alcohol misuse.[81] Results indicated that 36% of the sample were misusing neither of these substances, 38% were misusing opioids alone, 3% were misusing alcohol alone, and 23% were misusing both opioids and alcohol. Further, individuals who were misusing opioids with or without alcohol misuse were significantly more distressed and disabled in comparison to the group who was not misusing either substance. Given the substantial proportions of misuse in this previous work, there is a clear need to determine if these proportions replicate in other samples, particularly those of known risk for substance use disorders, such as US veterans. The present study sought to address this need by examining opioid and alcohol misuse in a sample of veterans who were prescribed opioids for the treatment of chronic pain. We used an existing clinical database to emulate the methods used in our previous study[81] by evaluating screening results for opioid and alcohol misuse, categorizing participant responses according to misuse status, and examining differences in functioning based on misuse status.

Methods

Participants

Data were collected from 211 consecutive veterans attending an initial appointment at an outpatient clinic for patients prescribed opioids for the treatment of chronic pain. The service accepted referrals from primary care and specialty chronic pain services where patients were prescribed an opioid medication for the treatment of chronic pain. Patients were referred to behavioral therapies for chronic pain, and in cases where misuse was identified, appropriate intervention to minimize risk of harm was provided (eg, opioid education, prescription management). Data were collected between 2014 and 2017. As part of the clinic's standard practice, participants completed a battery of self-report questionnaires prior to attending their appointment. The New Mexico VA Healthcare system Institutional Review Board provided an approval for waived consent (Consent #: 19-H289), which allowed the use of patient anonymized data for the purposes of the present study. With regard to formal inclusion criteria for the present study, the nature of the clinic ensured that all assessed patients provided data that were eligible for inclusion. Specifically, all individuals assessed were enrolled as a patient in the New Mexico VA Healthcare system, had a diagnosis of chronic pain, and were in receipt of an opioid prescription for the treatment of chronic pain.

Most participants were male (85%) who identified as non-Hispanic White (52.9%). The remaining individuals identified their race/ethnicity as: Hispanic (36.2%), Native American (4.8%), African American (3.8%), Asian American (0.5%), or other (2.9%). Average age was 54.8 years (*SD*: 13.3) and average education was 14.1 years (*SD*: 2.4). With regard to relationship status, most individuals were married or co-habitating (61.6%), followed by divorced or separated (25.1%), never married (8.5%), and widowed (4.8%). Only a minority were currently employed (23%) and approximately one-third were receiving payment for a military-service related disability (ie, service connection) (35%). Average pain duration was 13.6 years (*SD*: 11.2). Primary pain sites were as follows: low back (59.7%), lower extremity (16.1%), shoulders/neck (9.9%), middle back (3.8%), head (2.8%), upper extremity (2.4%), and other (5.3%).

Measures

As part of their assessment appointment, participants were asked to complete a battery of self-report questionnaires, as well as provide demographic and pain-related information. Usual pain intensity over the preceding week was assessed using an 11 point numeric rating scale, which ranged from 0 (no pain) to 10 (worst pain possible).

Opioid misuse. The seventeen item Current Opioid Misuse Measure (COMM)[12] was used to screen for opioid misuse. The COMM's items evaluate aspects of opioid use, cognitive difficulties, and emotional functioning (eg, anger). Each item is rated on a scale of frequency ranging from 0 ("never") to 4 ("very often") over the preceding 30 days. The recommended cut-score for opioid misuse is 9 or greater.[11,12] This cut score was associated with adequate sensitivity and specificity, both of which were .71, in relation to a positive classification on the Aberrant Drug Behavior Index, a

composite index of self-reported, clinician-reported, and urine toxicology findings in relation to opioid use.[11] Internal consistency in the present sample was acceptable, Cronbach's α = .81.

Alcohol misuse. The 3-item Alcohol Use Disorders Identification Test - Consumption (AUDIT-C)[9] was used to screen for alcohol misuse. The items of the AUDIT-C evaluate frequency and amount of alcohol consumption. The AUDIT-C is widely used and has a robust evidence base with regard to its utility as a screening measure for problematic alcohol use.[35,39] The recommended cut-score for alcohol misuse is 3 for women and 4 for men.[9,61] This cut score is associated with adequate sensitivity and specificity for alcohol misuse, which are a sensitivity of .86 and .73 in men and women, respectively, and specificity of .89 and .91 in men and women, respectively. Internal consistency in the present sample was acceptable, Cronbach's α = .80.

Depression. The 9 item patient Health Questionnaire (PHQ-9)[37] was used to assess symptoms of depression. The measure's 9 items assess frequency of symptom experience on a 0 ("not at all") to 3 ("nearly every day") scale over the preceding 2 weeks. The psychometric properties of the measure are well established[48] and it has been shown to have excellent specificity and sensitivity for Major Depressive Disorder diagnoses identified via structured clinical interview in those with chronic pain.[13] Internal consistency in the present sample was acceptable, Cronbach's α = .87.

Pain Catastrophizing. The thirteen item Pain Catastrophizing Scale (PCS)[70] was used to assess the frequency of catastrophic thinking about pain. Pain catastrophizing is reliably related to greater pain-related distress and disability.[49,68,78] Items are rated on a 0 ("not at all") to 4 ("all the time") scale with higher scores indicating greater frequency of catastrophic thoughts. Internal consistency in the present sample was acceptable, Cronbach's α = .93

Post-Traumatic Stress Disorder. The 20 item Post-Traumatic Stress Disorder Check List 5 (PCL-5; civilian version)[82] was used to evaluate for symptoms of PTSD. The items of the PCL-5 evaluate severity of symptoms experienced on a scale of 0 ("not at all") to 4 ("extremely"). Internal consistency in the present sample was acceptable, Cronbach's α = .96.

Analytic Approach

The analytic approach expanded upon that used by Vowles et al. (2018),[81] which used a community sample to evaluate rates of alcohol and opioid misuse in those with chronic pain prescribed opioids. Analyses consisted of 3 primary steps. First, cut-scores for the COMM and AUDIT-C were used to categorize individuals into 1 of 4 groups: 1) neither opioid nor alcohol misuse, 2) both opioid and alcohol misuse, 3) only opioid misuse, and 4) only alcohol misuse. Second, a multivariate analysis of variance (MANOVA) was conducted to examine between group differences in demographic (ie, gender, years of education, employment status) and pain-related (ie, average weekly pain intensity, pain duration, service connection status) characteristics. Where indicated by a significant omnibus MANOVA effect, one way follow-up ANOVAs were conducted for each variable. When significant, ANOVAs were followed by pairwise comparisons using a Bonferroni correction to help control for Type I error. Any variables that differed significantly across groups were retained as covariates in the next step, a second MANOVA examining between group differences in measures of psychosocial functioning, including depression, pain catastrophizing, and PTSD symptom severity. As with the preceding step, a significant omnibus MANOVA effect was followed by one way ANOVAs and, when significant, by Bonferroni-controlled pairwise comparisons.

Using the G*Power software,[18] a sample size of at least 68 individuals was required to detect a medium effect (f^2 =.15, alpha = .05) with 4 groups at a power of .95. A sample size of at least 472 was required to detect a small effect (f^2 = .02, alpha .05) with a power of .95. Using the present sample of 211, a sensitivity analysis using the same software indicated that our analyses could detect an effect within a 4 group model as small as f^2 = .05 with a power of .95.

Results

The proportion of veterans in each substance use category was as follows: 32.2% (n = 68) no misuse of alcohol or opioids, 23.2% (n = 49) opioid and alcohol misuse, 39.3% (n = 83) opioid misuse alone, and 5.2% (n = 11) alcohol misuse alone. Because of the small number of individuals misusing alcohol alone, these individuals were excluded from the subsequent MANOVA analyses.

Our initial MANOVA examined group differences across demographic and pain-related characteristics, including gender, age, years of education, employment status, average weekly pain intensity, pain duration, and service connection status. See Table 1 for details. The omnibus effect was just short of significance, Wilks Lambda = .87, P = .054, partial eta2 = .065. Given how close results were to significance, we elected to examine the follow-up one-way ANOVAs, which were significant only for age, F (2, 206) = 5.0, P < .01, partial eta2 = .053. As also shown in Table 1, Bonferroni-controlled pairwise comparisons indicated that the no misuse group was older than the misuse of both opioids and alcohol group. All other ANOVAs were non-significant, all F (2, 206) < 1.7, all P > .18, all partial eta2 < .019. Given these results, age was included as a covariate in the ensuing MANCOVA examining group differences based on included measures of psychosocial functioning.

The subsequent MANCOVA results indicated a significant omnibus effect, Wilks Lambda = .14, P < .001, partial eta2 = .63. Age was a significant covariate, Wilks Lambda = .89, P < .01, partial eta2 = .11. Follow-up one-way analyses were significant for all variables, F (2, 206) > 16.0, all P < .001, range partial eta2 = .19 - .70. Follow-up pairwise analyses using Bonferroni correction indicated a consistent overall pattern of group differences

Table 1. Means (SDs) or Percentages for Demographic and Pain-Related Variables

	Risk Group Classification				
Dependent Measure*	No misuse risk (N = 68)	Opioid & alcohol misuse risk (N = 49)	Opioid misuse risk (N = 83)	Alcohol misuse risk† (N = 11)	Full Sample (N = 211)
Gender (% male)	80.9%	87.8%	85.5%	100%	85.3%
Age (y)‡	57.6 (11.1)§	49.19 (13.7)¶	53.6 (14.4)§,¶	60.4 (12.1)	54.2 (13.5)
Education (y)	14.4 (2.7)	14.3 (2.2)	14.2 (2.2)	13.7 (3.3)	14.2 (2.4)
Pain Duration (y)	14.4 (13.3)	14.3 (10.2)	12.5 (9.3)	13.7 (15.5)	13.6 (11.2)
Average Pain (past wk)	6.8 (2.0)	6.6 (1.7)	6.9 (1.6)	5.8 (2.0)	6.7 (1.8)
Service Connection (% yes)	83.1%	91.5%	91.4%	81.8%	88.2%

*Average Pain was measured using a numeric rating scale (0 – 10).
†The alcohol misuse risk group was not included in the MANOVA comparisons due to the small sample size of the group.
‡P ≤ .05 for oneway ANOVA.
§, ¶Different superscripts indicate significantly different pairwise comparisons at the between-group level using a Bonferroni-controlled alpha.

such that participants who were not misusing either alcohol or opioids had scores indicating less distress and difficulty in comparison to those using misusing opioids alone or in combination with alcohol. The exception to this finding was for PTSD symptoms for which veterans who were misusing both opioids and alcohol had higher PCL-5 scores than the other 2 groups. Opioid misuse alone had higher PCL-5 scores than those with no misuse reported. See Table 2 for descriptive information and Supplementary Table 1 for estimated marginal means for the 3 groups included in the MANCOVA after controlling for participant age.

Discussion

Co-occurring chronic pain and problematic substance use is an important issue, as increasing evidence indicates it is prevalent in a clinically significant proportion of individuals and its impacts can be severe.[31,85] To date, the risks associated with opioid misuse and Opioid Use Disorder (OUD) in the treatment of chronic pain are well-established,[5,16,25] but risks associated with misuse of other substances is relatively less studied.[65,77,85] Alcohol misuse is particularly relevant given the widespread availability of alcohol, significant risks associated with its misuse, and synergistic effects with other central nervous system depressants thereby increasing risk of overdose.[8,40,60,64,67,71,75] This study examined self-reported opioid and alcohol misuse rates in a sample of veterans prescribed opioids for the treatment of chronic pain.

In particular, we sought to examine whether previous findings indicating high rates of concomitant misuse of opioids and alcohol in a community sample[81] were comparable to rates in a treatment-seeking sample. Perhaps the most noteworthy finding from the present study is the substantial concordance with this previous work, as the proportions are almost identical. Specifically, the percentages from the previous study and the present 1, respectively, were as follows: 36% and 32% were not misusing either substance, 38% and 39% were misusing opioids, 3% and 5% were misusing alcohol, and 23% and 23% were misusing both opioids and alcohol. Given that the participants across the 2 studies were quite different, as the previous study involved community dwelling individuals who were paid to complete an online survey (via Amazon's Mechanical Turk; MTURK) and the present study included veterans completing an assessment for treatment, the degree of agreement in findings is striking and bolsters confidence in the reliability of the findings. Further, the combined sample size across studies is 342, suggesting that these findings may be generalizable to other settings as well. Additional corroborating evidence for generalizability comes from a recently published study of almost 66,000 US Veterans with OUD, which found that 41% had OUD only, 23% had OUD plus 1 additional Substance Use Disorder (SUD), and 26% had OUD and 2 or

Table 2. Means (SDs) for Primary Study Variables

	Risk Group Classification				
Dependent Measure*	No misuse risk (N = 68)	Opioid & alcohol misuse risk (N = 49)	Opioid misuse risk (N = 83)	Alcohol misuse risk† (N = 11)	Full Sample (N = 211)
Pain Catastrophizing**	20.6 (12.5)§	32.4 (9.6)¶	31.3 (10.0)¶	17.1 (9.6)	27.3 (12.1)
Depression**	8.7 (6.2)§	14.5 (6.5)¶	13.7 (5.9)¶	8.5 (6.0)	11.98 (6.7)
PTSD Symptoms**	19.3 (16.1)§	48.3 (14.8)‖	36.7 (18.4)¶	12.6 (13.4)	32.2 (20.3)

*Pain catastrophizing was measured using the Pain Catastrophizing Scale (PCS), depression was measured using the Patient Health Questionnaire 9 (PHQ-9), PTSD Symptoms were measured using the PTSD Checklist for DSM-5 (PCL-5).
†The alcohol misuse risk group was not included in the MANOVA comparisons due to the small sample size of the group.
**P ≤ .001 for oneway ANCOVA.
§, ¶, ‖Different superscripts indicate significantly different pairwise comparisons at the between-group level using a Bonferroni-controlled alpha.

more SUDs.[42] The most commonly occurring SUD in this study was AUD, 41%. In brief, opioid misuse/OUD appears to co-occur with other forms of substance misuse with substantial frequency.

As noted in the introduction, the use of opioids in the treatment of chronic pain is complex as opioids are associated with potential for both risk *and* harm.[2,28,47] Furthermore, a clinically significant minority of opioid-treated individuals with chronic pain engage in risky opioid use behaviors.[7,50,76,79] As noted, while the risks of opioid use in the treatment of chronic pain have been well documented, several other important issues remain opaque in this population.

First, alcohol is the most used sedative in the world with 86% of adults reporting lifetime use and 70% reporting use in the past year in the 2019 report of the Substance Abuse and Mental Health Services Administration.[63] Furthermore, harmful alcohol use is common and is associated with substantial risk of morbidity and mortality.[8,25,40,60,64,67,71,75,86] Yet, in chronic pain assessment and treatment settings, it has not historically been regularly assessed or treated.[32,85] In retrospect, this seems a substantial oversight. For example, the neurobiology of both chronic pain and harmful alcohol use (eg, Alcohol Use Disorder) are interrelated in terms of etiological and neurobiological factors.[21,45,46]

Further, a recent study found that chronic pain is frequent amongst individuals seeking treatment for alcohol use, 54%, and that the presence of chronic pain increases the risk of delayed treatment seeking.[10] Finally, while alcohol has analgesic properties and is used by upwards of 28% of chronic pain sufferers for pain relief,[62] guidance from the National Institute on Alcohol Abuse and Alcoholism indicate that the dose required is likely to exceed moderate drinking guidance, thereby increasing risk of alcohol-related complications.[56] We would argue that alcohol misuse requires at least as much scientific investigation as opioid misuse, yet a PubMed search (dated May 23, 2022) for "chronic pain" and either "opioid" or "alcohol" indicated 9026 publications for the former and 969 for the latter, a ratio of approximately 9:1. This discrepancy deserves to be addressed, as it seems out of proportion to the gravity of this situation, particularly given the results in the present work and elsewhere that indicate significant risk of co-use in opioid prescribed individuals.

Second, while the problem of comorbid chronic pain and substance use disorders/ substance misuse is firmly established in the clinical and scientific literature, there are few treatment options at present that seek to offer a coherent and coordinated approach. It is likely that these 2 clinical issues are too inter-related and complex to be addressed separately, eg, with separate chronic pain and substance use treatments, as their co-occurrence interferes with the effective treatment of either condition individually.

To our knowledge, while several studies have highlighted the use of behavioral treatments or active patient management to reduce opioid misuse in those with chronic pain,[33,57,58,69] there are only a handful of treatment trials that have evaluated integrated behavioral treatments that offer integrated approaches seeking to simultaneously address both pain interference and opioid misuse. Some examples of such integrated treatment include cognitive behavioral therapy (CBT) approaches that have not indicated significant treatment effects,[4,26] the Mindfulness Oriented Recovery (MORE) approach of Garland and colleagues,[22,23] and an integrated treatment consisting of Acceptance and Commitment Therapy and Mindfulness-Based Relapse Prevention (ACT+MBRP) by our group.[80] Clearly there is room to expand this work through further examination of CBT, other approaches such as MORE and ACT+MBRP, as well as interventions that integrate a focus on alcohol misuse. Finally, there is a need to examine these issues in substance use disorder populations. For example, a recent study by Ilgen and colleagues[31] evaluated the efficacy of a behavioral pain management intervention within a residential SUD treatment program and found effects on pain intensity and pain tolerance, while there were no effects for pain-related functioning or substance use. To our knowledge, the Ilgen et al study is the first study of its kind and breaks new ground in an area sorely in need of development, particularly in the pursuit of reductions in both pain's interference on life and in substance misuse frequency.

Third and finally, the results of this and our previous study[81] primarily indicate that differences across measures are present only between the no misuse groups and misuse groups (specifically including opioid misuse alone and opioid/alcohol misuse in combination). That finding was unexpected, as it was hypothesized that co-morbid opioid and alcohol misuse would be associated with worse scores on measures than misuse of opioids alone. The sole exception across the 2 studies was the finding for PTS symptoms, as the co-morbid misuse group noted greater symptoms in this area than the opioid only misuse group. While these studies have been cross-sectional in nature, meaning that any conclusions regarding causality are only hypothetical, the pattern of findings suggests that opioid misuse may be a hypothetical key driver of the differences observed. Any additional disruption of alcohol misuse may not be significant enough to be detectable statistically. These hypotheses will need to be examined in longitudinal or experimental work to test them more adequately. If opioid misuse is found to be the primary "driver" of disrupted functioning, then that will go some distance towards helpfully identifying key issues for treatment to address.

There are limitations to this work. First, the nature of these data is important to consider, as they are cross-sectional and self-report in nature. Thus, causality cannot be inferred and measurement error or bias may be present. More broadly, we did not have access to all variables possibly related to misuse, including opioid treatment details (eg, dose, duration), pain or substance use disorder treatment history, or history of mental or physical health diagnoses. The screening measures used in relation to opioid and alcohol use may not identify cases with complete accuracy, particularly given that

baserates matter in the accuracy of prediction.[3] Furthermore, while the substance use disorder literature indicates moderate to strong concordance between self-reported and actual substance use,[51,55,59] there is evidence this concordance may be lower in people using opioids in an aberrant manner.[1,30,84] Finally, these data were collected at assessment from veterans with chronic pain who had been referred to a specialist chronic pain treatment service. Therefore, further examination of the generalizability of these findings to individuals without these same characteristics is warranted.

Second, there are considerations in relation to the COMM and AUDIT-C specifically – both measures include frequency items, while the COMM also includes items assessing emotional aspects. Third, the rate of alcohol misuse alone was so small (n = 11; 5% of total sample) that we elected to exclude it from group comparisons. While this proportion is consistent with our previous study, it does limit the amount of information regarding these individuals.

In closing, these data indicate the need for further work in the area of substance misuse in those with chronic pain. While much attention recently has been paid to opioid-related morbidity and mortality in those with chronic pain, substance misuse issues are not limited to opioids alone. In fact, while opioid misuse is the third most common contributor to morbidity and mortality globally of any SUD, it trailed behind alcohol, which is the second most common.[14] The complexity of treating chronic pain is well-known and the exponential increases in opioid prescription over the past few decades in many countries seems to have increased this complexity. We may be at a turning point in the field, where pain treatments can incorporate the knowledge from the SUD field and apply them in an empirically sound manner to both effectively treat opioid misuse/OUD, but also integrate evidence based assessments and treatments for other SUDs. We suggest that now is a crucial time for this expansion and integration.

Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.jpain.2022.06.003.

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