Syndemic interactions of chronic pain, mental health problems, and opioid misuse and their association with academic performance and quality of life among college students

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ABSTRACT

Background: College students experience multiple stressors impacting academic performance and quality of life (QoL), including chronic pain, mental health issues, and opioid misuse, which can co-occur and exacerbate one another. Guided by syndemic theory, this study examined the associations between these three health conditions and academic performance and QoL.
Methods: We analyzed cross-sectional data from 334,957 students from the ACHA-NCHA III survey (2019–2022). Lifetime chronic pain and mental health problems were self-reported based on provider diagnosis or symptoms. Opioid misuse was defined as ever using heroin or using prescription opioids for nonmedical purposes. Syndemic burden was measured using individual indicators, a composite count (0–3), and interactions terms. Academic performance was measured via a binary indicator of impeded performance, and QoL was assessed using a weighted average score from four validated WHOQOL-BREF domains. Multiple logistic and linear regression were used, adjusting for demographic and contextual variables.
Results: Greater syndemic burden was associated with worse outcomes. Students with all three conditions had the highest odds of impeded academic performance (aOR = 7.38, 95 % CI: 6.52, 8.35) and the lowest QoL scores ($\widehat{\beta}_{ADJ} = -12.05$, 95 % CI: -12.37, -11.73). Each factor was independently associated with adverse outcomes, and significant interaction effects, especially when mental health problems were present, suggested syndemic amplification.
Conclusion: These findings support a syndemic framework linking chronic pain, mental health problems, and opioid misuse with academic and QoL outcomes in college students. Interventions should prioritize integrated mental health services and non-pharmacological pain management options in college health systems.

1. Introduction

College students face a wide range of stressors related to academic demands and environmental changes, and during this time, academic performance and quality of life can be impacted by various factors, including chronic pain, mental health problems, and opioid misuse. Chronic pain, a persistent or recurrent pain lasting longer than 3 months (Treede et al., 2015), affects 7.4 % of college students (American College Health Association, 2022) and has been shown to negatively impact quality of life, class attendance, and school performance (McCarthy et al., 2021). Mental health problems are a significant issue on college campuses, with 60.8 % of students reporting anxiety, 46.9 % reporting high stress, and 44.3 % reporting depression (Gorman et al., 2021).

Multiple studies find depression and ADHD to be negatively associated with academic performance (Asher BlackDeer et al., 2023; Riboldi et al., 2022; Prevatt and Young, 2014) and the presence of any mental health problem to be negatively associated with quality of life among young adults (Evans et al., 2007; Liu et al., 2020; Ribeiro et al., 2018). Opioid misuse, the use of illicit/non-prescription and prescription opioids, has decreased from 5.4 % in 2013 to 2.7 % in 2018 among college students, (National Institute on Drug Abuse) yet opioid misuse continues to negatively affect college students' academic performance (Ellis et al., 2020; Harries et al., 2018; Meshesha et al., 2017) and quality of life (Rhee and Rosenheck, 2019). Chronic pain, mental health problems, and opioid misuse can coexist for a college student and further exasperate the effects each has on academic performance and quality of life. This

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clustering of two or more diseases or health conditions and their interactions that lead to an increased health burden is explained by Singer's syndemic theory (Singer et al., 2017).

The Syndemic Theory was first proposed by Merrill Singer, a medical anthropologist investigating a cluster of substance abuse, violence, and AIDS cases in Hartford, Connecticut in the early 1990s. He observed that HIV was more prevalent in inner cities where substance abuse and violence were interlinked. He defined the interactions between substance abuse, violence, and AIDS (SAVA) as a "closely interrelated complex of health and social crises." (Singer, 1994) Higher SAVA scores were associated with higher viral loads and reduced effectiveness of treatments (Singer et al., 2017). Singer later identified three criteria necessary to properly characterize a syndemic: the clustering of two or more diseases or health conditions, the biological interactions among the conditions leading to an increased health burden, and contextual factors creating conditions for the interactions to lead to worsened health outcomes (Singer et al., 2017). Few studies incorporating the syndemic theory have focused on college students (Orchowski et al., 2018; Shi et al., 2019; Turpin et al., 2023), and these studies lacked either one or two criteria identified by Singer. College students represent a uniquely vulnerable group due to the transitional nature of this life stage, which is often marked by increasing independence, identity formation, and exposure to new stressors. This period of emerging adulthood is also characterized by heightened experimentation, particularly in social and substance use behaviors, and by academic and performance pressures that can exacerbate both mental and physical health challenges. For example, the drive to succeed academically or athletically may heighten the risk of chronic pain, especially among student-athletes. These contextual features of the college experience may intensify the clustering and interaction of chronic pain, mental health problems, and opioid misuse, warranting application of syndemic theory in this setting.

Despite increasing recognition that college students experience high rates of chronic pain, mental health problems, and substance use, prior research has largely examined these conditions in isolation. Existing studies tend to focus on individual associations with academic or quality of life outcomes rather than their combined or interacting effects. Only a handful of studies have applied syndemic theory to college student populations, and most fall short of examining all three of Singer's criteria, clustering, interaction, and contextual drivers (Orchowski et al., 2018; Shi et al., 2019; Turpin et al., 2023). No prior research, to our knowledge, has rigorously quantified the combined and interactive effects of chronic pain, mental health problems, and opioid misuse on functional outcomes such as academic performance and quality of life in a national college student sample. There is therefore a need to apply the Syndemic Theory and its three criteria to college students, including an investigation into the interactions of chronic pain, mental health problems, and opioid misuse in American academic institutions.

Previous research has shown that the interactions of two or more of the selected health conditions (i.e., chronic pain, mental health problems, and opioid misuse) can lead to worsened health outcomes. For instance, the relationship between opioid misuse and mental illness has been shown to be bidirectional with their coexistence being linked to worse treatment outcomes, higher morbidity and mortality, and higher risk of suicide compared to those with only one of the conditions (Martins et al., 2009; Silva, 2023). Similarly, the relationship between chronic pain and mental health problems is bi-directional (Hooten, 2016; Yao et al., 2023), leading to a lower quality of life together (Van Rijswijk et al., 2019). Relating to Singer's third criterion, contextual factors create environments that exacerbate the effects of these interactions on college campuses. Among chronic pain patients, for instance, opioid misuse is more likely for younger groups (18–30) compared to older individuals (Edlund et al., 2014), and interpersonal relationships are shown to have significant relationships with chronic pain (McCarthy et al., 2021; Hadi et al., 2019) and mental illness (Evans et al., 2007) among young adults. Welsh, Shentu, and Sarvey (2019) found that students affiliated with fraternities were more likely to have substance use disorder, mental health issues, and lower GPAs as well as experiencing peer pressure and chronic illness (Welsh et al., 2019). Qeadan et al. (2022) found that discrimination is positively associated with all mental health symptoms (Qeadan et al., 2022). The interactions between chronic pain, mental health problems, and opioid misuse, while considering relevant contextual factors on college campuses, demonstrate a complex and dangerous interplay that requires further attention.

The objective of the current study is therefore to determine whether syndemic effects exist between chronic pain, mental health problems, and opioid misuse, such that their interactions are associated with worsened academic performance and quality of life among college students. Using data from the American College Health Association (ACHA) National College Health Assessment (NCHA), a nationally recognized health and research survey, this study aims to quantify both the summative and interactive syndemic effect of the three selected health conditions on academic performance and quality of life, while adjusting for relevant societal and environmental predictors, including interpersonal relationships, racial perceptions, and college environments. Per Singer's syndemic theory, it is hypothesized that the clustering of chronic pain, mental health problems, and opioid misuse will be associated with worsened outcomes among college students compared to each health condition alone.

2. Methods

2.1. Data source, sample, and design

Data for this study were obtained from the ACHA-NCHA survey constructed for Fall 2019 to Fall 2022, referred to as the ACHA-NCHA III (Lederer and Hoban, 2022). The ACHA-NCHA III is a national, biannual survey administered to millions of students across 973 academic institutions. The survey is filled out physically or electronically by students and asks about a wide range of health behaviors and attitudes, including alcohol, tobacco, and other drug use, sexual health, mental health, physical health, personal safety and violence, food insecurity and homelessness, student characteristics (i.e., GPA, enrollment status, type of institution attended, and fraternity/sorority involvement), and demographic characteristics (i.e., age, gender identity, sexual orientation, and race/ethnicity). This study therefore follows a cross-sectional design. Institutions voluntarily elect to participate in the ACHA-NCHA, and administration protocols, including census versus random sampling, are determined at the institutional level. The ACHA does not apply post-stratification weights to the national dataset, and thus, according to ACHA guidance, generalizability may be limited due to institutional self-selection and variability in campus-level response rates. For this study, data were aggregated from Fall 2019 to Fall 2022, including a total of 334,957 student responses.

2.2. Measures

2.2.1. Dependent variables

2.2.1.1. Impeded academic performance. The first outcome of interest was a dichotomized indication (yes/no) of whether one's academic performance was impeded. Students were asked, "Within the last 12 months, have any of the following affected your academic performance?" Students reported if specific instances or conditions, including assault, allergies, anxiety, depression, headaches/migraines, etc. had impeded their academic performance. For each specific instance or condition, students had four options. Students who answered "I have experienced this issue, and it negatively impacted my performance in a class" or "I have experienced this issue and it delayed progress towards my degree" for any of the instances or conditions were assigned an indication of "Yes" for impeded academic performance. This definition

is consistent with previous studies (Edwards and Froehle, 2023; Vernet and Sberna, 2022).

2.2.1.2. Quality of life. The second outcome of interest, quality of life (QoL), was constructed by adapting questions from the ACHA-NCHA III and aligning them with the abbreviated version of the World Health Organization quality of life instrument (WHOQOL-BREF) (WHO, 1998). The score was made up of four domains: physical health, psychological, social relationships, and environment. Items from the NCHA were identified for each facet of the four domains to create a QoL scale that imitates the WHOQOL-BREF scale (Supplement Table 1). Each item was used on a 5-point Likert scale, with 5 indicating the highest QoL. Missing data ranged from 0.6 % to 5.4 % across domains and was determined to be missing completely at random (MCAR) per Little's test (Little, 1988). Data were therefore imputed with a single, fully conditional specification using the discriminant function. Domain specific scores were created using principal component analysis (PCA), wherein all principal components with eigenvalues over 1 were included and weighted by their variance contribution (Zhang et al., 2018). An overall weighted average QoL score was then constructed to incorporate each domain with appropriate weighting determined by performing a random forest analysis and using the ratio of importance scores relative to the lowest. The overall QoL score was rescaled to a 0–100 scale, following the WHOQOL-BREF scale (Harper et al., 1999; Skevington and Tucker, 1999). Cronbach's alpha for the adapted overall QoL scale demonstrated excellent internal consistency (raw $\alpha = 0.90$; standardized $\alpha = 0.92$).

2.2.2. Independent variables

2.2.2.1. Syndemic factors. The primary predictors of interest were the syndemic factors: chronic pain, mental health problems, and opioid misuse (all dichotomous (yes/no) variables). Students were asked if they had ever been diagnosed with chronic pain, and students who answered "Yes" were assigned an indication of "Yes" for chronic pain. Students were assigned an indication of "Yes" for mental health problems if at least one of the following was satisfied: (1) binary indication (yes/no) for mental illness diagnosis, (2) a Kessler 6 Scale score of thirteen or greater (Kessler et al., 2010; Prochaska et al., 2012), (3) a UCLA 3-Item Loneliness Scale score of six or greater (Russell et al., 1980), (4) a Suicide Behavior Questionnaire-Revised Screening score greater than six (Osman et al., 2001), (5) a Diener Flourishing Scale score less than 36 (Diener et al., 2010), or (6) a Connor-Davison Resilience Scale Score less than six (Vaishnavi et al., 2007). This definition was chosen to reflect various mental health problems, including panic attacks, phobias, schizophrenia, depression, etc., as well as feelings of hopelessness, being overwhelmed, exhaustion, loneliness, sadness, anxiety, and anger. Students were assigned an indication of "Yes" for opioid misuse if they had ever used heroin or prescription opioids for a nonmedical use.

2.2.2.2. Syndemic conditions. To assess the burden of increasing health conditions, syndemic conditions were represented as a composite variable summing the 3 binary syndemic factors (i.e., chronic pain, mental health problems, and opioid misuse). The variable was constructed following previous studies by adding the number of syndemic factors experienced by each student (O'Leary et al., 2014; Zhang et al., 2019). The syndemic condition variable thus ranged from 0 to 3, in which 0 meant a student had none of the conditions and 3 meant a student had all conditions.

2.2.2.3. Syndemic interactions. A variable for syndemic interactions extends the syndemic conditions variable to convey the effect corresponding to each condition combination. Variations of the syndemic interaction variable included no conditions, chronic pain only, mental health problems only, opioid misuse only, chronic pain and mental health problems only, chronic pain and opioid misuse only, mental

health problems and opioid misuse only, and interaction of all three conditions.

2.2.2.4. Cofactors of interest. Demographic predictors of interest were age (i.e. 18-20, 21–24, 25–29, 30+), gender identity (i.e. cisgender female, cisgender male, gender diverse, transgender), sexual orientation (i.e., heterosexual, gay/lesbian, bisexual, other), race/ethnicity (i.e. American Indian/Alaska Native, Hispanic or Latino/a/x, Non-Hispanic Asian or Asian American, Non-Hispanic Biracial or Multiracial, Non-Hispanic Black, Non-Hispanic Other, Non-Hispanic White, and Native Hawaiian or Pacific Islander), survey year (2019 through 2022), US geographic region (i.e., Midwest, Northeast, South, and West), type of institution (i.e. 2-year or 4 or more years), enrollment status (i.e., full-time or part-time), average weekly hours spent on academics (i.e., $\leq$ 5, >5–10, >10–15, >15–20, >20), housing (i.e., on-campus, off-campus, unhoused, other), and insurance status (i.e., private, public, uninsured, don't know). Survey year was included to adjust for temporal variation, including potential effects of the COVID-19 pandemic on student health and academic outcomes. The number of interpersonal problems faced by a student was also adjusted for, encompassing issues with family, friends, peers, roommates, intimate relationships, and/or coping with the health problems or death of someone close to the student (i.e., 0, 1, 2, $\geq$ 3). Binary indications of sorority/fraternity involvement and relationship status were also included as social predictors of interest (Welsh et al., 2019).

2.3. Statistical analysis

Descriptive statistics were used to describe the sociodemographic characteristics of the sample overall and stratified by syndemic factors and conditions. To visually describe the sample, the overlap of the syndemic factors was calculated and presented in a Venn diagram. While the total sample size (334,957) is reported, it should be noted that inferential analyses were conducted on only complete cases. Multiple imputation, assuming a multivariate normal distribution on 10 iterative sets, was conducted and compared to complete case analysis to ensure robustness of findings. Results revealed similar findings.

The outcomes were presented across each primary predictor (syndemic factors, conditions, and interactions). Associations between predictors and outcomes were assessed through multiple logistic regression for academic performance and multiple linear regression for QoL. Odds ratios (ORs) and beta-hats ($\widehat{\beta}$) with 95 % CIs were calculated to represent these associations. Each of the syndemic predictors, including the binary factor indications, their sum of conditions occurring, and their formal interaction categories, was fit individually with outcomes as well as adjusted for cofactors of interest. Formal interactions were tested between all syndemic factors (chronic pain, mental health problems, and opioid misuse). This included all two-way and three-way interactions totaling eight models with the two outcomes. All models were adjusted for cofactors of interest.

Goodness-of-fit (GOF) for logistic regression was assessed visually with Pearson and Deviance residuals and tested formally with Hosmer and Lemeshow's test, Stukel's test, and Osius and Rojek's test. Influential observations were assessed with DFBETAS. GOF for linear regression was assessed with residual diagnostics and influential observations were assessed with Cook's distance (D). Multicollinearity, for both models, was examined using Variance Inflation Factor (VIF) analysis with VIFs of 10 or higher indicating multicollinearity. The predictive ability of models was assessed with the area under the receiver operating characteristic (ROC) curve (AUC) for logistic regression and R^2 for linear regression. AUC and R^2 were calculated across all models and were used to assess if models accounting for interactions exhibited greater predictive ability than without. All hypothesis tests were two-sided with a significance level of 5 %. SAS version 9.4 (SAS Institute, INC) was used for all analyses.

3. Results

Table 1 shows the characteristics of participants by syndemic factors (opioid misuse, chronic pain, and mental health problems). Of the 334,957 students included in this study, 4.0 % (13,386) reported opioid misuse, 7.1 % (23,249) reported a diagnosis of chronic pain, and 75.8 % (252,042) reported a diagnosis of a mental illness or significant feelings of sadness, loneliness, or stress. Fig. 1 displays the overlap of syndemic factors with 0.04 % (121) of students having reported opioid misuse and chronic pain only, 2.88 % (9,424) reported opioid misuse and mental health problems only, 5.63 % (18,453) reported mental health problems and chronic pain only, and 0.63 % (2,066) reported all three conditions. All characteristics were significantly different between syndemic factor and condition groups (Table 1 and Supplement Table 2). Pertaining to the outcomes, 57.3 % (189,500) of students reported impeded academic performance, and the mean (SD) QoL score was 84.5 (9.7) (Table 2).

3.1. Syndemic factors

Table 2 shows the associations between syndemic factors and outcomes. Mental health problems had the strongest association with the outcomes. Students with mental health problems had higher odds of impeded academic performance (aOR = 3.19, 95 % CI: 3.13, 3.25) and lower average QoL ($\widehat{\beta}_{ADJ} = -8.48$, 95 % CI: −8.54, −8.42) compared to those without mental health problems. Students with chronic pain showed higher odds of impeded academic performance (aOR = 2.10, 95 % CI: 2.03, 2.18) and lower average QoL ($\widehat{\beta}_{ADJ} = -1.34$, 95 % CI: −1.44, −1.24) compared to students without chronic pain. Students who engaged in opioid misuse had higher odds of impeded academic performance (aOR = 1.28, 95 % CI: 1.23, 1.34) and lower average QoL ($\widehat{\beta}_{ADJ} = -1.77$, 95 % CI: −1.90, −1.65) compared to students who had not engaged in opioid misuse.

3.2. Syndemic conditions

Table 2 shows the associations between the outcomes and the composite variable summing the three binary syndemic factors (syndemic conditions). Compared to students with none of the syndemic factors, as the number of syndemic conditions increased (1–3), the odds of impeded academic performance also increased (**1**: aOR: 3.14, 95 % CI: 3.08, 3.20; **2**: aOR: 5.68, 95 % CI: 5.48, 5.88; **3**: aOR: 7.38, 95 % CI: 6.52, 8.35). Compared to students with none of the syndemic factors, as the number of syndemic conditions increased (1–3), average QoL scores continually declined (**1**: $\widehat{\beta}_{ADJ} = -8.21$, 95 % CI: −8.27, −8.15; **2**: $\widehat{\beta}_{ADJ} = -9.97$, 95 % CI: −10.07, −9.87; **3**: $\widehat{\beta}_{ADJ} = -12.05$, 95 % CI: −12.37, −11.73).

3.3. Syndemic interactions

Table 2 also shows the associations between the seven interactions of the syndemic factors (chronic pain only, mental health only, opioid misuse only, chronic pain & mental health only, chronic pain & opioid use only, mental health & opioid use only, and the interaction of all three). The interaction of two or more syndemic factors produced higher odds of impeded academic performance and larger declines in average QoL compared to syndemic factors alone, with mental health problems having a strong effect on the interactions. The interaction of chronic pain and mental health problems only had higher odds of impeded academic performance (aOR = 6.82, 95 % CI: 6.52, 7.12) and larger declines in average QoL ($\widehat{\beta}_{ADJ} = -9.89$, 95 % CI: −10.01, −9.77) than mental health problems or chronic pain alone. The interaction of mental health problems and opioid misuse only also resulted in higher odds of impeded academic performance (aOR = 4.21, 95 % CI: 4.00, 4.44) and larger declines in average QoL ($\widehat{\beta}_{ADJ} = -10.27$, 95 % CI: −10.42, −10.11) than mental health problems or opioid misuse alone. Chronic

pain and opioid misuse alone showed moderate associations with academic performance, but the interaction of chronic pain and opioid misuse only showed increased odds of impeded academic performance (aOR: 2.73, 95 % CI: 1.86, 4.00). However, the interaction of chronic pain and opioid misuse had an insignificant association with QoL ($\widehat{\beta}_{ADJ} = -0.87$, 95 % CI: −2.12, 0.38). The interaction of all three syndemic factors produced the highest odds of impeded academic performance (aOR: 7.30, 95 % CI: 6.45, 8.26) and the lowest average QoL ($\widehat{\beta}_{ADJ} = -12.00$, 95 % CI: −12.32, −11.69).

Table 3 shows the adjusted associations between the two-way and three-way interactions of the syndemic factors and the outcomes. Two-way interactions showed little deviations in the adjusted odds of impeded academic performance, but compounded effects were seen for QoL scores. Mental health problems again had a significant effect. Students with chronic pain had significantly lower average QoL when mental health problems were also present ($\widehat{\beta}_{ADJ} = -1.54$, 95 % CI: −1.66, −1.43) compared to when they were not ($\widehat{\beta}_{ADJ} = -0.19$, 95 % CI: −0.36, −0.02). A similar effect was seen for opioid misuse, such that students reporting opioid misuse had significantly lower average QoL when they also experienced mental health problems ($\widehat{\beta}_{ADJ} = -1.97$, 95 % CI: −2.11, −1.82) compared to when they did not ($\widehat{\beta}_{ADJ} = -0.92$, 95 % CI: −1.14, −0.71). The presence of either chronic pain or opioid misuse for a student experiencing mental health problems also affected QoL. A student experiencing mental health problems had lower average QoL when chronic pain was also present ($\widehat{\beta}_{ADJ} = -9.15$, 95 % CI: −9.50, −8.79) compared to when it was not ($\widehat{\beta}_{ADJ} = -8.52$, 95 % CI: −8.58, −8.46). The same effect was seen for the interaction between mental health problems and opioid misuse, such that students experiencing mental health problems had lower average QoL when opioid use was also present ($\widehat{\beta}_{ADJ} = -9.04$, 95 % CI: −9.49, −8.59) than when it was not ($\widehat{\beta}_{ADJ} = -8.52$, 95 % CI: −8.58, −8.46).

Mental health also had a significant effect on the three-way interactions. For students with chronic pain, experiencing mental health problems but not opioid misuse was associated with a lower average QoL ($\widehat{\beta}_{ADJ} = -1.42$, 95 % CI: −1.54, −1.31) compared to experiencing only chronic pain ($\widehat{\beta}_{ADJ} = -0.19$, 95 % CI: −0.37, −0.02). The added experience of opioid misuse without mental health problems for students with chronic pain was associated with relatively no change in average QoL ($\widehat{\beta}_{ADJ} = -0.03$, 95 % CI: −0.91, 0.86) compared to chronic pain only, yet the addition of both mental health problems and opioid misuse resulted in the lowest average QoL among students with chronic pain ($\widehat{\beta}_{ADJ} = -2.09$, 95 % CI: −2.52, −1.66). For students misusing opioids, experiencing mental health problems but not chronic pain resulted in lower average QoL ($\widehat{\beta}_{ADJ} = -1.83$, 95 % CI: −1.99, −1.67) than for opioid misuse alone ($\widehat{\beta}_{ADJ} = -0.94$, 95 % CI: −1.16, −0.72). Although the addition of chronic pain but not mental health problems for students misusing opioids was not associated with a significantly different average QoL ($\widehat{\beta}_{ADJ} = -0.56$, 95 % CI: −1.41, 0.28), the presence of both mental health problems and chronic pain was associated with the lowest average QoL among students misusing opioids ($\widehat{\beta}_{ADJ} = -2.05$, 95 % CI: −2.46, −1.64). For students experiencing mental health problems, average QoL was lowered with the addition of chronic pain alone ($\widehat{\beta}_{ADJ} = -9.06$, 95 % CI: −9.42, −8.71) and opioid misuse alone ($\widehat{\beta}_{ADJ} = -8.96$, 95 % CI: −9.41, −8.51) compared to mental health problems alone ($\widehat{\beta}_{ADJ} = -8.48$, 95 % CI: −8.54, −8.42). While the presence of both chronic pain and opioid misuse among students experiencing mental health problems resulted in a lower average QoL ($\widehat{\beta}_{ADJ} = -8.90$, 95 % CI: −10.75, −7.05) compared to mental health problems alone, this reduction was not significant and smaller than those of the addition of either chronic pain or opioid misuse alone.

Table 1
Demographic characteristics of college students in the U.S by syndemic factors.

	Total n (%d)	Opioid misuse[a]			Chronic pain[b]			Mental health problems[c]		
		No n (%e)	Yes n (%e)	p-value[f]	No n (%e)	Yes n (%e)	p-value[f]	No n (%e)	Yes n (%e)	p-value[f]
Total	334,957 (100)	318,254 (96.0[g])	13,386 (4.0[g])		305,263 (92.9[g])	23,249 (7.1[g])		80,678 (24.3[g])	252,042 (75.8[g])	
Age				<0.001			<0.001			<0.001
18–20 years	146,285 (44.4)	142,793 (45.4)	3038 (23.0)		137,638 (45.4)	7347 (31.9)		32,968 (41.3)	113,278 (45.5)	
21–24 years	105,050 (31.9)	100,904 (32.1)	3770 (28.6)		97,606 (32.2)	6464 (28.1)		25,311 (31.7)	79,699 (32.0)	
25–29 years	41,485 (12.6)	38,847 (12.2)	2480 (18.8)		37,849 (12.5)	3197 (13.9)		10,851 (13.6)	30,617 (12.3)	
30+ years	36,344 (11.0)	32,274 (10.3)	3905 (29.6)		29,983 (9.9)	6024 (26.1)		10,668 (13.4)	25,665 (10.2)	
Gender identity				<0.001			<0.001			<0.001
Cisgender female	215,469 (65.0)	207,370 (65.4)	7316 (55.1)		196,529 (64.5)	16,719 (72.0)		48,242 (60.0)	167,143 (66.6)	
Cisgender male	103,486 (31.2)	97,906 (30.9)	5107 (38.5)		97,839 (32.1)	4506 (19.4)		31,572 (39.2)	71,837 (28.6)	
Gender diverse	11,167 (3.4)	10,369 (3.3)	734 (5.5)		9279 (3.0)	1742 (7.5)		534 (0.7)	10,623 (4.2)	
Transgender	1383 (0.4)	1259 (0.4)	118 (0.9)		1128 (0.4)	232 (1.0)		45 (0.1)	1337 (0.5)	
Sexual orientation				<0.001			<0.001			<0.001
Heterosexual	251,788 (76.2)	242,167 (76.7)	8701 (65.7)		234,072 (77.0)	15,099 (65.3)		72,386 (90.3)	179,283 (71.7)	
Gay/Lesbian	13,606 (4.1)	12,804 (4.1)	749 (5.7)		12,261 (4.0)	1199 (5.2)		1851 (2.3)	11,746 (4.7)	
Bisexual	37,039 (11.2)	34,658 (11.0)	2234 (16.8)		33,043 (10.9)	3688 (15.9)		3683 (4.6)	33,350 (13.3)	
Other	27,984 (8.5)	26,290 (8.2)	1557 (11.8)		24,538 (8.1)	3152 (13.6)		2247 (2.8)	25,723 (10.3)	
Race				<0.001			<0.001			<0.001
AI/AN[h]	6981 (2.1)	6388 (2.0)	559 (4.2)		6078 (2.0)	832 (3.6)		1468 (1.8)	5507 (2.2)	
Hispanic or Latino/a/x	48,073 (14.3)	46,142 (14.5)	1769 (13.2)		44,852 (14.7)	2757 (11.9)		11,310 (14.0)	36,742 (14.6)	
NH[i] Asian or Asian American	46,284 (13.7)	45,399 (14.2)	629 (4.7)		44,067 (14.4)	1517 (6.5)		11,752 (14.6)	34,487 (13.7)	
NH[i] Biracial or multiracial	17,360 (5.2)	16,722 (5.3)	851 (6.4)		16,100 (5.3)	1330 (5.7)		3755 (4.7)	13,870 (5.5)	
NH[i] Black	17,640 (5.2)	15,976 (5.0)	494 (3.7)		15,345 (5.0)	984 (4.1)		4453 (5.5)	12,107 (4.8)	
NH[i] Other	10,871 (3.2)	8386 (2.6)	413 (3.0)		7094 (2.3)	597 (2.6)		2062 (2.6)	6738 (2.7)	
NH[i] White	187,997 (56.1)	178,734 (56.2)	8642 (64.6)		171,233 (56.1)	15,190 (65.3)		45,727 (56.7)	142,203 (56.3)	
Native Hawaiian or Pacific Islander	539 (0.2)	507 (0.2)	29 (0.2)		494 (0.2)	42 (0.2)		151 (0.2)	388 (0.2)	
Survey Year				<0.001			<0.001			<0.001
2019	38,679 (11.6)	36,780 (11.6)	1676 (12.5)		35,607 (11.76)	2486 (10.7)		10,749 (13.3)	27,768 (11.0)	
2020	63,680 (19.0)	60,554 (19.0)	2702 (20.2)		58,384 (19.1)	4405 (19.0)		16,615 (20.6)	46,829 (18.6)	
2021	129,693 (38.7)	122,474 (38.5)	5351 (40.0)		118,115 (38.7)	8435 (36.3)		30,336 (37.6)	98,019 (38.9)	
2022	102,905 (30.7)	98,446 (30.9)	3657 (27.3)		93,157 (30.5)	7923 (34.0)		22,978 (28.5)	79,426 (31.5)	
US Geographic Region				<0.001			<0.001			<0.001
Midwest	73,421 (21.9)	70,472 (22.1)	2424 (18.1)		67,461 (22.1)	4812 (20.7)		18,662 (23.1)	54,458 (21.6)	
Northeast	74,230 (22.1)	71,625 (22.5)	1961 (14.7)		68,232 (22.4)	4540 (19.5)		17,829 (22.1)	55,991 (22.2)	
South	98,367 (29.4)	93,003 (29.2)	3915 (29.2)		89,092 (29.1)	6833 (29.4)		24,489 (30.4)	72,722 (28.9)	
West	88,939 (26.6)	83,154 (26.2)	5086 (38.0)		80,478 (26.4)	7064 (30.4)		19,698 (24.4)	68,871 (27.3)	
Type of institution				<0.001			<0.001			<0.001
2-year	11,578 (3.5)	10,695 (3.4)	808 (6.0)		10,147 (3.3)	1220 (5.3)		2477 (3.1)	9061 (3.6)	
4 or more years	323,379 (96.5)	307,559 (96.6)	12,578 (94.0)		295,116 (96.7)	22,029 (94.7)		78,201 (96.9)	242,981 (96.4)	
Enrollment status				<0.001			<0.001			<0.001
Full-time	300,973 (91.5)	288,760 (91.8)	10,991 (83.8)		278,065 (91.9)	19,688 (86.0)		72,549 (90.9)	228,252 (91.7)	
Part-time	28,045 (8.5)	25,806 (8.2)	2123 (16.2)		24,512 (8.1)	3213 (14.0)		7283 (9.1)	20,742 (8.3)	

Table 1 (*continued*)

	Total			P			P			P
Average weekly hours spent on academics[j]				<0.001			<0.001			<0.001
≤ 5	21,309 (6.4)	19,902 (6.3)	1230 (9.3)		19,214 (6.4)	1684 (7.3)		5000 (6.2)	16,188 (6.5)	
>5–10	78,171 (23.6)	74,032 (23.4)	3627 (27.3)		71,352 (23.5)	5631 (24.4)		18,001 (22.5)	59,878 (23.9)	
>10–15	103,695 (31.2)	99,146 (31.4)	3887 (29.3)		95,291 (31.4)	6936 (30.1)		24,878 (31.0)	78,479 (31.4)	
>15–20	75,543 (22.8)	72,327 (22.9)	2682 (20.2)		69,214 (22.8)	5128 (22.2)		18,958 (23.7)	56,277 (22.5)	
≥20	52,879 (16.0)	50,580 (16.0)	1846 (13.9)		48,060 (15.9)	3703 (16.0)		13,325 (16.6)	39,265 (15.7)	
Part of fraternity/sorority				0.7520			0.0012			<0.001
No	304,489 (91.9)	291,044 (91.9)	12,184 (91.8)		279,782 (91.8)	21,424 (92.4)		73,163 (91.2)	231,137 (92.1)	
Yes	26,985 (8.1)	25,773 (8.1)	1090 (8.2)		24,905 (8.2)	1755 (7.6)		7749 (28.8)	19,766 (7.9)	
Housing				<0.001			<0.001			<0.001
On-campus	116,922 (35.0)	112,072 (35.2)	2536 (19.0)		107,042 (35.1)	5935 (25.6)		27,266 (33.9)	87,615 (34.8)	
Off-campus	212,097 (63.4)	200,830 (63.2)	10,340 (77.3)		193,340 (63.4)	16,448 (70.9)		51,922 (64.4)	160,023 (63.6)	
Unhoused	1626 (0.5)	1416 (0.5)	199 (1.5)		1371 (0.5)	224 (1.0)		180 (0.2)	1439 (0.6)	
Other	3780 (1.1)	3478 (1.1)	290 (2.2)		3135 (1.0)	606 (2.5)		1191 (1.5)	2585 (1.0)	
Relationship status				<0.001			<0.001			<0.001
Single	172,307 (52.0)	166,118 (52.4)	5453 (41.1)		160,107 (52.6)	10,246 (44.2)		34,928 (43.5)	137,269 (54.7)	
Partnered	159,102 (48.0)	150,640 (47.6)	7815 (58.9)		144,515 (47.4)	12,938 (55.8)		45,402 (56.5)	113,595 (45.3)	
Insurance status				<0.001			<0.001			<0.001
Private	288,604 (88.1)	277,112 (88.5)	10,349 (78.6)		266,890 (88.6)	18,660 (81.0)		71,823 (90.4)	216,596 (87.4)	
Public	26,265 (8.0)	24,200 (7.7)	1975 (15.0)		22,442 (7.5)	3562 (15.5)		5068 (6.4)	21,185 (8.5)	
Uninsured	10,078 (3.1)	9292 (3.0)	737 (5.6)		9247 (3.1)	711 (3.1)		2084 (2.6)	7978 (3.2)	
Don't know	2652 (0.8)	2530 (0.8)	100 (0.8)		2525 (0.8)	92 (0.4)		469 (0.6)	2180 (0.9)	
No. of interpersonal problems				<0.001			<0.001			<0.001
0	84,421 (25.5)	82,015 (25.9)	2148 (16.2)		80,484 (26.4)	3024 (13.0)		33,863 (42.1)	50,546 (20.1)	
1	73,822 (22.3)	71,301 (22.5)	2295 (17.2)		68,880 (22.6)	4219 (18.2)		20,345 (25.3)	53,466 (21.3)	
2	66,305 (20.0)	63,498 (20.0)	2616 (19.7)		60,841 (19.9)	4869 (21.0)		13,636 (16.9)	52,666 (21.0)	
≥3	106,891 (32.2)	100,269 (31.6)	6222 (46.9)		94,776 (31.1)	11,106 (47.8)		12,584 (15.7)	94,297 (37.6)	

[a] Opioid misuse includes illicit/non-prescription and prescription opioids.

[b] Chronic pain includes those with a diagnosis of chronic pain.

[c] Mental health problems includes those with a diagnosis of at least one mental health conditions and/or those reporting significant feelings of hopelessness, loneliness, and sadness.

[d] n = Sample size; Not all counts add up to total because of missing values.

[e] Column percentage.

[f] Chi-square test for independence; Highlighted P-values indicate statistical insignificance at the 5 % significance level.

[g] %'s out of total (n = 334,957).

[h] American Indian/Alaska Native.

[i] Non-Hispanic.

[j] Average of hours spent in a typical week attending classes and hours spent studying.

3.4. Contextual factors

Supplement Figs. 1 and 2 show the adjusted characteristic associations with impeded academic performance and QoL as responses. Gender diverse and transgender students had significantly higher odds of impeded academic performance and lower average QoL compared to cisgender males. Bisexual, gay/lesbian, and students of unlisted sexual orientations faced similar worsened outcomes compared to heterosexual students. American Indian/Alaska Native (AI/AN), biracial/multiracial, and students of unlisted races had worse outcomes compared to Non-Hispanic White students. Unhoused and uninsured students also faced poorer outcomes compared to students living on campus and students with private insurance, respectively. Each additional interpersonal problem further increased the odds of impeded academic performance and significantly reduced average QoL.

4. Discussion

This study is the first to evaluate whether syndemic effects exist between the three selected health conditions (i.e., chronic pain, mental health problems, and opioid misuse) and academic performance and quality of life among college students. Our findings reveal a syndemic effect, wherein the interactions of the three conditions exacerbate negative outcomes for college students. This analysis further expands the existing literature by applying the syndemic theory to college students, which few have done thus far (Orchowski et al., 2018; Shi et al., 2019; Turpin et al., 2023). Additionally, unlike previous research on syndemics among college students, this analysis utilized both a
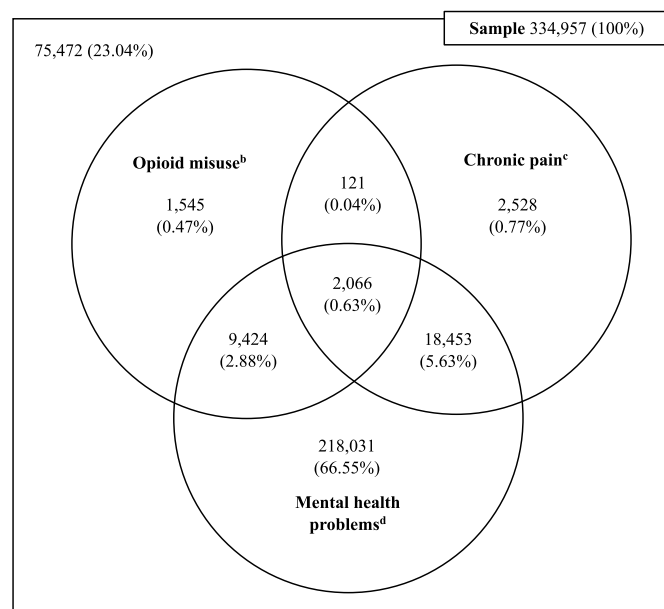
Fig. 1. Venn Diagram[a]for opioid misuse, chronic pain, and mental health problems
[a] Each value is presented *n* (%). Not all counts add up to total because of missing values. [b] Opioid misuse includes illicit/non-prescription and prescription opioids. [c] Chronic pain includes those with a diagnosis of chronic pain. [d] Mental health problems includes those with a diagnosis of at least one mental health condition and/or those reporting significant feelings of hopelessness, loneliness, and sadness.

summative and interactive variable to accurately depict syndemic interactions (Tsai, 2018). Although our findings of a syndemic effect cannot be compared to earlier studies, individual relationships between our syndemic factors and the outcomes are consistent with previous research (McCarthy et al., 2021; Asher BlackDeer et al., 2023; Riboldi et al., 2022; Prevatt and Young, 2014; Evans et al., 2007; Liu et al., 2020; Ribeiro et al., 2018; Ellis et al., 2020; Harries et al., 2018; Meshesha et al., 2017; Rhee and Rosenheck, 2019). Mental health problems affected nearly 75 % of college students in our study, which is consistent with the National Healthy Minds Study (Lipson et al., 2022a). The prevalence of opioid misuse (4 %) and chronic pain (7 %) were consistent with recent national studies on college students as well (National Health Interview Survey, 2019; Patrick et al., 2022). Overall, the findings of this study are in a comparable range to past research.

4.1. Interplay and amplification of syndemic factors

The relationship between chronic pain, mental health problems, and opioid misuse in this analysis aligns with Merrill Singer's syndemic theory (Singer et al., 2017). First, there is a clustering of two or more health conditions, shown by the nearly 10 % of college students in this sample experiencing any combination of chronic pain, mental health problems, and opioid misuse. This clustering is a cycle of suffering for college students, illustrated by the interplay between the health conditions. For instance, college students with chronic pain often experience heightened psychological issues due to the physical and emotional toll of their condition, including impaired functioning, sleep disruptions, and social isolation (Serbic et al., 2020, 2021). Additionally, students with chronic pain or mental health difficulties may seek solace in substance use, including opioid misuse (Welsh et al., 2019; Groenewald et al., 2019). Opioid misuse can then lead to an increased risk of mental health difficulties (Martins et al., 2009) and an eventual increase in pain for chronic pain patients (Carpenter et al., 2019), thereby creating a harmful cycle between chronic pain, mental health problems, and opioid

misuse.

Satisfying the second criterion of the syndemic theory, the interactions among the three health conditions lead to an increased health burden, shown by both a decline in academic performance and quality of life. The combined presence of chronic pain, mental health problems, and opioid misuse is therefore a syndemic on college campuses and should be treated as such. A syndemic requires a deviation from the traditional healthcare approach of treating these conditions separately and calls for an integrated strategy that considers the complex interactions between the three health conditions (Singer et al., 2017). It has been noted that syndemics mainly exist theoretically, and it is challenging to implement the theory practically (Weaver and Kaiser, 2022), but institutions can begin by understanding these complex interactions and what specific drivers may exist in their local and societal environments (Mendenhall et al., 2022).

Significant characteristic associations were observed with the outcomes, fulfilling the third criterion of the syndemic theory that contextual factors create conditions for the syndemic interactions to lead to worsened health outcomes. Minority student populations, including gender minority, sexual minority, and racial minority students, as well as students struggling with housing, health insurance, and interpersonal problems experienced increased odds of impeded academic performance and reduced average QoL. Marginalization has been identified as a contextual factor to worsen syndemic effects in past literature, citing drivers such as discrimination, stigma, and systemic racism, homophobia, and transphobia (Quinn et al., 2021; Wesp et al., 2019; Williams and Vermund, 2021). Much research incorporating the syndemic theory has also explored the compounding effects of homelessness and financial stress, as each are barriers to obtaining care (Bromberg et al., 2020; Mendenhall et al., 2017; Quinn et al., 2018). Additionally, past evidence has found that increasing interpersonal problems can negatively affect each facet of the syndemic identified in this study (Qeadan et al., 2021; Sun, 2023; Wickramaratne et al., 2022). By considering the contextual factors that may worsen the syndemic of chronic pain, mental health problems, and opioid misuse among college students, institutions can bolster their efforts in combatting it.

4.2. Mental health as a central factor

The findings of this study underscore the profound impact of mental health on academic and life quality aspects, with mental health problems being associated with the worst outcomes in this study. Special attention should therefore be focused on improving mental health resources in college environments. Notable barriers to mental health services on college campuses exist, including trouble recognizing symptoms, a preference for self-reliance, and a lack of time (Ebert et al., 2019; Gulliver et al., 2010). One of the most significant barriers identified across studies, however, is the stigma around mental health (Ebert et al., 2019; Gulliver et al., 2010; Turosak and Siwierka, 2021). Hurtful remarks from fellow students and staff on campus, misunderstandings about mental illness, and the difficulty in separating stigma from the lived experiences of mental illness are all stigma-related barriers to mental health services voiced by college students (Turosak and Siwierka, 2021). Institutions can combat these sources of stigma by raising awareness of mental health problems often faced by college students to mitigate the influence of mental health problems on worsening academic performance and quality of life (Stuart, 2016).

4.3. Chronic pain management in college students

Chronic pain was associated with reduced academic functioning and quality of life, which is consistent with previous literature (Serbic et al., 2021). A possible driver of these relationships is the lack of social interactions commonly experienced by students with chronic pain (Serbic et al., 2020), which is similarly associated with decreased mental well-being (Wickramaratne et al., 2022) and reduced academic

Table 2
Odds of outcomes by predictors and their syndemic interactions.

	Impeded academic performance[a]				Quality of life[b]			
	Unadjusted		Adjusted[c]		Unadjusted		Adjusted[c]	
	n[d] (%[e])	OR (95 % CI)	aOR (95 % CI)	AUC	Mean (SD)	Beta (95 % CI)	aBeta (95 % CI)	R²
Overall	189,500 (57.3[f])	–	–	–	84.5 (9.7)	–	–	–
Syndemic factors				0.761				0.453
Chronic pain[g]								
No	169,781 (55.7)	Ref.	Ref.		84.9 (9.3)	Ref.	Ref.	
Yes	18,037 (77.6)	2.76 (2.68, 2.85)	2.10 (2.03, 2.18)		80.8 (10.7)	−4.03 (−4.16, −3.91)	−1.34 (−1.44, −1.24)	
Mental illness[h]								
No	24,102 (30.0)	Ref.	Ref.		93.2 (4.9)	Ref.	Ref.	
Yes	165,371 (66.0)	4.52 (4.44, 4.60)	3.19 (3.13, 3.25)		81.8 (8.9)	−11.46 (−11.53, −11.40)	−8.48 (−8.54, −8.42)	
Opioid misuse[i]								
No	179,723 (56.8)	Ref.	Ref.		84.7 (9.4)	Ref.	Ref.	
Yes	9073 (68.4)	1.65 (1.59, 1.71)	1.28 (1.23, 1.34)		80.5 (10.9)	−4.18 (−4.35, −4.02)	−1.77 (−1.90, −1.65)	
Syndemic conditions[j]				0.759				0.444
0	22,119 (29.3)	Ref.	Ref.		93.3 (4.8)	Ref.	Ref.	
1	141,647 (63.8)	4.25 (4.18, 4.33)	3.14 (3.08, 3.20)		82.4 (8.6)	−10.94 (−11.00, −10.87)	−8.21 (−8.27, −8.15)	
2	21,803 (77.9)	8.50 (8.23, 8.78)	5.68 (5.48, 5.88)		79.7 (9.9)	−13.63 (−13.74, −13.52)	−9.97 (−10.07, −9.87)	
3	1695 (82.2)	11.16 (9.95, 12.50)	7.38 (6.52, 8.35)		76.7 (12.3)	−16.60 (−16.96, −16.25)	−12.05 (−12.37, −11.73)	
Syndemic interactions				0.761				0.453
None	22,119 (29.3)	Ref.	Ref.		93.3 (4.8)	Ref.	Ref.	
Chronic pain only	1192 (47.2)	2.15 (1.99, 2.33)	2.10 (1.93, 2.29)		92.7 (5.1)	−0.59 (−0.90, −0.26)	−0.10 (−0.38, 0.18)	
Mental health only	139,947 (64.2)	4.33 (4.25, 4.41)	3.18 (3.12, 3.25)		82.2 (8.6)	−11.13 (−11.19, −11.06)	−8.41 (−8.47, −8.35)	
Opioid misuse only	508 (32.9)	1.18 (1.06, 1.31)	1.23 (1.09, 1.38)		92.2 (5.2)	−1.04 (−1.45, −0.64)	−0.87 (−1.23, −0.51)	
Chronic pain & mental health only	15,030 (81.5)	10.59 (10.18, 11.03)	6.82 (6.52, 7.12)		79.6 (9.9)	−13.66 (−13.78, −13.53)	−9.89 (−10.01, −9.77)	
Chronic pain & opioid misuse only	57 (47.1)	2.15 (1.50, 3.07)	2.73 (1.86, 4.00)		92.6 (5.8)	−0.71 (−2.13, 0.72)	−0.87 (−2.12, 0.38)	
Mental health & opioid misuse only	6716 (71.4)	6.00 (5.72, 6.29)	4.21 (4.00, 4.44)		79.6 (9.7)	−13.74 (−13.91, −13.57)	−10.27 (−10.42, −10.11)	
Chronic pain, mental health, & opioid misuse	1695 (82.2)	11.16 (9.95, 12.50)	7.30 (6.45, 8.26)		76.7 (12.3)	−16.60 (−16.95, −16.25)	−12.00 (−12.32, −11.69)	

Highlighted results indicate insignificance.

[a] Academic performance is impeded when participants identified any qualifying indication as negatively impacting performance in a class or delaying progress towards degree.

[b] QoL is a 0–100 scale with higher scores indicating higher QoL. The measure was constructed from various Likert scales from 4 domains: physical, social, environmental, and mental.

[c] Syndemic factors and conditions were adjusted by age, gender identity, sexual orientation, race, survey year, geographic region, type of institution, enrollment status, involvement in a fraternity or sorority, insurance status, relationship status, housing type, number of hours spent on academics, and a count of interpersonal problems.

[d] n = Frequency; Not all counts add up to total because of missing values.

[e] Row percentage.

[f] %'s out of total (n = 334,957).

[g] Chronic pain includes those with a diagnosis of chronic pain.

[h] Mental illness includes those with a diagnosis of at least one mental health condition and/or those reporting significant feelings of hopelessness, loneliness, and sadness.

[i] Opioid misuse includes illicit/non-prescription and prescription opioids.

[j] Participants were grouped by whether they fit the criteria for none, one, two, or three of the syndemic factors.

performance (Senter, 2024). Simply promoting increased social interactions among these students, however, may put them at risk of substance use initiation, a common social practice in college settings (Welsh et al., 2019). Since students with chronic pain are already at an increased risk for abusing substances (Welsh et al., 2019; Serbic et al., 2021), institutions should ensure these students are socially adjusting to college without falling into unhealthy relationships involving repeated substance use. College advisors can be a source for students with chronic pain to collaborate with to learn about clubs or groups aligned with their

interests to foster positive peer relationships (Houman and Stapley, 2013). Improving social support for students with chronic pain can eliminate a driver of developing or worsening mental health symptoms and opioid misuse, diminishing this syndemic effect on college campuses.

4.4. Opioid misuse and its implications

In this study, opioid misuse included both prescription and illicit use,

Table 3
Odds/betas of outcomes by predictors and their interactions.

	Impeded academic performance[a]			Quality of life score[b]		
	OR (95 % CI)	aOR[c] (95 % CI)	AUC	Beta (95 % CI)	aBeta[c] (95 % CI)	R^2
Two-way interactions						
Chronic pain[d]						
Chronic pain Yes v. No at Mental health = Yes	2.43 (2.34, 2.52)	2.12 (2.04, 2.21)	0.760	−2.73 (−2.85, −2.60)	−1.54 (−1.66, −1.43)	0.452
Chronic pain Yes v. No at Mental health = No	2.14 (1.98, 2.31)	2.10 (1.93, 2.29)		−0.57 (−0.76, −0.39)	−0.19 (−0.36, −0.02)	
Chronic pain Yes v. No at Opioid misuse = Yes	2.11 (1.88, 2.36)	1.90 (1.68, 2.16)	0.733	−3.77 (−4.26, −3.29)	−2.48 (−2.90, −2.06)	0.318
Chronic pain Yes v. No at Opioid misuse = No	2.76 (2.67, 2.85)	2.33 (2.25, 2.42)		−3.82 (−3.95, −3.69)	−2.01 (−2.12, −1.90)	
Mental health[e]						
Mental health Yes v. No at Chronic pain = Yes	4.96 (4.56, 5.39)	3.23 (2.95, 3.54)	0.760	−13.37 (−13.77, −12.97)	−9.15 (−9.50, −8.79)	0.452
Mental health Yes v. No at Chronic pain = No	4.37 (4.29, 4.45)	3.20 (3.14, 3.26)		−11.22 (−11.28, −11.15)	−8.52 (−8.58, −8.46)	
Mental health Yes v. No at Opioid misuse = Yes	5.33 (4.78, 5.94)	3.48 (3.10, 3.92)	0.757	−13.36 (−13.86, −12.85)	−9.04 (−9.49, −8.59)	0.452
Mental health Yes v. No at Opioid misuse = No	4.46 (4.39, 4.54)	3.24 (3.18, 3.30)		−11.33 (−11.40, −11.27)	−8.52 (−8.58, −8.46)	
Opioid misuse[f]						
Opioid misuse Yes v. No at Chronic pain = Yes	1.19 (1.07, 1.33)	1.18 (1.04, 1.33)	0.733	−3.64 (−4.11, −3.18)	−2.45 (−2.85, −2.04)	0.318
Opioid misuse Yes v. No at Chronic pain = No	1.57 (1.50, 1.63)	1.44 (1.38, 1.51)		−3.68 (−3.86, −3.51)	−2.45 (−2.61, −2.30)	
Opioid misuse Yes v. No at Mental health = Yes	1.44 (1.38, 1.50)	1.34 (1.28, 1.40)	0.757	−3.03 (−3.20, −2.87)	−1.97 (−2.11, −1.82)	0.452
Opioid misuse Yes v. No at Mental health = No	1.21 (1.09, 1.34)	1.24 (1.11, 1.39)		−1.01 (−1.24, −0.77)	−0.92 (−1.14, −0.71)	
Three-way interactions						
Chronic pain[d]						
Chronic pain Yes v. No at Mental health = Yes and Opioid misuse = Yes	1.86 (1.65, 2.10)	1.73 (1.52, 1.98)	0.761	−2.87 (−3.35, −2.38)	−2.09 (−2.52, −1.66)	0.453
Chronic pain Yes v. No at Mental health = Yes and Opioid misuse = No	2.45 (2.36, 2.54)	2.14 (2.05, 2.23)		−2.53 (−2.66, −2.40)	−1.42 (−1.54, −1.31)	
Chronic pain Yes v. No at Mental health = No and Opioid misuse = Yes	1.82 (1.25, 2.64)	2.22 (1.49, 3.31)		0.34 (−0.63, 1.31)	−0.03 (−0.91, 0.86)	
Chronic pain Yes v. No at Mental health = No and Opioid misuse = No	2.15 (1.99, 2.33)	2.10 (1.93, 2.29)		−0.59 (−0.78, −0.39)	−0.19 (−0.37, −0.02)	
Mental health[e]						
Mental health Yes v. No at Chronic pain = Yes and Opioid misuse = Yes	5.20 (3.58, 7.56)	2.67 (1.79, 3.99)	0.761	−15.90 (−18.11, −13.69)	−8.90 (−10.75, −7.05)	0.453
Mental health Yes v. No at Chronic pain = Yes and Opioid misuse = No	4.93 (4.52, 5.37)	3.25 (3.96, 3.57)		−13.07 (−13.46, −12.68)	−9.06 (−9.42, −8.71)	
Mental health Yes v. No at Chronic pain = No and Opioid misuse = Yes	5.08 (4.53, 5.70)	3.43 (3.03, 3.88)		−12.69 (−13.19, −12.20)	−8.96 (−9.41, −8.51)	
Mental health Yes v. No at Chronic pain = No and Opioid misuse = No	4.33 (4.25, 4.41)	3.18 (3.12, 3.25)		−11.13 (−11.19, −11.06)	−8.48 (−8.54, −8.42)	
Opioid misuse[f]						
Opioid misuse Yes v. No at Chronic pain = Yes and Mental health = Yes	1.05 (0.94, 1.19)	1.07 (0.94, 1.22)	0.761	−2.95 (−3.41, −2.48)	−2.05 (−2.46, −1.64)	0.453
Opioid misuse Yes v. No at Chronic pain = Yes and Mental health = No	1.00 (0.69, 1.44)	1.30 (0.88, 1.92)		−0.12 (−1.05, 0.81)	−0.56 (−1.41, 0.28)	
Opioid misuse Yes v. No at Chronic pain = No and Mental health = Yes	1.39 (1.32, 1.45)	1.32 (1.26, 1.39)		−2.61 (−2.79, −2.43)	−1.83 (−1.99, −1.67)	
Opioid misuse Yes v. No at Chronic pain = No and Mental health = No	1.18 (1.06, 1.31)	1.23 (1.09, 1.38)		−1.04 (−1.29, −0.80)	−0.94 (−1.16, −0.72)	

Highlighted results indicate insignificance.

[a] Academic performance is impeded when participants identified any qualifying indication as negatively impacting performance in a class or delaying progress towards degree.

[b] QoL is a 0–100 scale with higher scores indicating higher QoL. The measure was constructed from various Likert scales from 4 domains: physical, social, environmental, and mental.

[c] Interactions were adjusted by age, gender identity, sexual orientation, race, survey year, geographic region, type of institution, enrollment status, involvement in a fraternity or sorority, insurance status, relationship status, housing type, number of hours spent on academics, a count of interpersonal problems, and any significant interactions between factors.

[d] Chronic pain includes those with a diagnosis of chronic pain.

[e] Mental illness includes those with a diagnosis of at least one mental health condition and/or those reporting significant feelings of hopelessness, loneliness, and sadness.

[f] Opioid misuse includes illicit/non-prescription and prescription opioids.

which each contributed to the negative outcomes identified in this study. Students who misuse prescription opioids are more likely to experience depressive symptoms, anxiety, chronic pain, and academic difficulties compared to those who don't (Kerr et al., 2023). Students who misuse prescription opioids are also more likely to use illicit opioids, such as heroin or fentanyl (Harries et al., 2018). Illicit opioid use is similarly associated with the negative outcomes of prescription opioid misuse but to a greater amount (Kerr et al., 2023). Opioid misuse, from prescription misuse to illicit use, therefore exists on a continuum of risk and their effects on academic performance and quality of life should be given focused attention at colleges and universities. Promoting healthy approaches to both physical and psychological pain management, for instance, can be especially helpful in mitigating the syndemic identified in this study (Voepel-Lewis et al., 2018). Non-opioid medications, counseling, physical exercise, and a balanced diet are all examples of health-promoting behaviors that can help students with chronic pain and mental health difficulties instead of turning to substance use.

4.5. Institutional infrastructure and implications

While our findings underscore the importance of addressing chronic pain, mental health problems, and opioid misuse as a syndemic, it is important to acknowledge that many academic institutions are poorly equipped to provide adequate prevention or treatment services for these conditions. Mental health services on college campuses are often underfunded, overburdened, and limited in scope, leading to long wait times, inconsistent follow-up, and reduced access to care, particularly for students with complex or co-occurring needs (Watkins et al., 2012; Lipson et al., 2022b). This mismatch between student health burdens and institutional capacity may exacerbate the impact of syndemic interactions on academic and quality of life outcomes.

Substance use, in particular, remains a neglected area in many college health systems. Institutional responses are frequently constrained by liability concerns, reputational risk, and limited institutional policies, contributing to an unspoken "don't ask, don't tell" culture regarding substance misuse (Wechsler et al., 2000; Arria and DuPont, 2010). These dynamics may discourage open disclosure and delay timely identification or intervention, especially among students engaged in nonmedical use of prescription opioids.

Even when physical health services are accessible, pain management options on campus are often constrained. Students, particularly student-athletes, may receive opioid prescriptions as a first-line response due to the convenience of pharmacological treatment in settings where integrated or multidisciplinary care is unavailable (American College Health Association, 2016; Pettegrew, 2021; Paskvan, 2021). This practice can inadvertently elevate the risk for opioid misuse, especially when more holistic pain management strategies (e.g., physical therapy, behavioral interventions) are not provided.

Institutional characteristics such as enrollment size, healthcare staffing, and resource availability likely shape both the prevalence and institutional response to syndemic health burdens. While the ACHA-NCHA dataset includes a direct measure of institutional enrollment size, we did not adjust for it in our models due to multicollinearity with related structural variables already included (institution type, region, and enrollment status). Future research should examine how institutional size and healthcare capacity interact with syndemic conditions to inform tailored policy and programmatic interventions that align student needs with institutional infrastructure.

4.6. Strengths and limitations

A strength of the current study is the size of the cohort, which was made possible by the ACHA-NCHA III. This study included 334,957 college students, which is the largest college student cohort in the literature on syndemics. An additional strength of the current study is the analysis of the syndemic effect through a composite and interactive variable. While a composite variable provides powerful insights into the cumulative burden of health conditions, an interactive variable more accurately depicts their interactions, a crucial criterion of the syndemic theory (Zhang et al., 2019; Tsai and Burns, 2015; Tsai et al., 2017). These findings provide an understanding of interacting conditions on US college campuses to advance health and social research, clinical care, and prevention.

Limitations exist, however, in the current study. Students and institutions self-select to be included in the survey, so the representativeness of the sample may be limited. Institutions voluntarily choose to participate in the ACHA-NCHA, and administration protocols (e.g., census vs. sample) vary across campuses. As the ACHA-NCHA III dataset is not weighted at the national level, generalizability to all U.S. college students is limited and may be influenced by institutional characteristics or response rates. Institution-level response rates are not pooled or reported nationally, and response rates vary considerably by campus. As a result, the extent of selection bias cannot be precisely quantified. Additionally, the use of self-reported data introduces the potential for various response biases. For instance, the prevalences of chronic pain and opioid misuse may be underestimated as students may not have a diagnosis for their chronic pain symptoms and may be hesitant to report opioid misuse due to social desirability bias. Our opioid misuse variable reflects lifetime use, as assessed through items based on the World Health Organization's ASSIST (Alcohol, Smoking and Substance Involvement Screening Test), a validated instrument for identifying substance-related risk. However, the measure does not distinguish between recent and more distant misuse, which may limit our ability to isolate current substance-related impairment. Nonetheless, any lifetime misuse of heroin or prescription opioids among college students remains a significant indicator of risk and dysfunction. The chronic pain measure reflects a lifetime diagnosis confirmed by a healthcare or mental health professional, which indicates a clinically recognized and likely impactful condition. However, the measure does not distinguish between current versus past symptoms or assess changes in pain severity over time. This may result in some misclassification or reduced specificity when interpreting its relationship to present-day academic or quality of life outcomes. Similarly, students were asked to self-report mental illness diagnoses, which may underestimate prevalence, but we believe that the inclusion of validated scales signifying moderate to severe feelings of sadness, loneliness, and stress helps reorient toward the population prevalence of mental health problems among college students. Mental health problems were assessed using a composite of diagnostic and symptom-based indicators. While this inclusive approach improves sensitivity, it may also conflate clinically distinct mental health conditions and symptom severity levels. Due to the cross-sectional nature of the current study, causal relationships cannot be determined. Future longitudinal studies should explore the numerous causal pathways between chronic pain, mental health problems, opioid misuse, academic performance, and quality of life among college students.

Although we adjusted for survey year to capture temporal variation during the COVID-19 pandemic, we were unable to account for specific pandemic-related exposures such as lockdown stringency, remote learning status, or COVID-specific psychological distress, which may have influenced both predictors and outcomes.

5. Conclusion

This study identified significant associations between chronic pain, mental health problems, and opioid misuse, both individually and interactively, with impeded academic performance and lower quality of life among college students. The findings are consistent with a syndemic framework and suggest that co-occurring health burdens may compound functional outcomes in this population. Although causal inferences cannot be drawn due to the study's cross-sectional design, the results underscore the need for future research that explores causal pathways and evaluates integrated prevention and support strategies tailored to

student populations.

CRediT authorship contribution statement

Ethics approval

Not required.

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Declaration of competing interest

Author declares they have no conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.socscimed.2025.118243.

Data availability

The data that support the findings of this study are available from the American College Health Association National College Health Assessment (ACHA-NCHA) (Contact Christine Kukich, at ckukich@acha.org).

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