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# Rx for addiction and medication safety: An evaluation of teen education for opioid misuse prevention

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1 ABSTRACT

2

3 Background: Rhode Island (RI) ninth graders report lifetime nonmedical use of prescription opioids  
4 (NMUPO) of 8.9%. NMUPO is associated with transition to heroin use, opioid overdose, and death.

5

6 Objectives: Measure changes in 9<sup>th</sup> grade students' knowledge, confidence, perceptions of opioid use  
7 disorder prevention, overdose response with naloxone, treatment, and recovery, following the delivery  
8 of an interactive substance use disorder curriculum.

9

10 Methods: Eight RI public high schools were recruited to participate. Freshman in each school were  
11 administered identical surveys that collected demographic data, substance use and misuse knowledge,  
12 students' perceptions of substance misuse harm, reported drug use, and risk and protective behaviors  
13 before and after the curriculum.

14

15 Results: Among 969 pre-intervention survey respondents, 19% reported use of marijuana, 3% heroin  
16 use, and 21% nonmedical use of prescription opioids. Between the pre-intervention to the post-  
17 intervention survey, significantly more students identified that addiction is a chronic brain disease (79%  
18 to 83%,  $p = 0.05$ ), drug users are not responsible for their addiction (81% to 88%,  $p = 0.001$ ), and that  
19 non-medical use of a prescription medication is use without a prescription (81% to 88%,  $p = 0.001$ ).

20 Improved confidence was also reported in identifying opioid withdrawal symptoms (26% to 45%,  $p <$   
21  $0.0001$ ), identifying signs of an opioid overdose from 29% to 46% ( $p < 0.0001$ ), and knowing when to  
22 administer naloxone (17% to 45%,  $p < 0.0001$ ). Confidence to refer someone to treatment improved  
23 from 31% to 45% ( $p < 0.0001$ ). Logistic regression showed associations between mental health, peer  
24 use, parental affection, and academic performance factors as related to NMUPO.

25

26 Conclusions: Students reported significant NMUPO prevalence. Ninth grade students' knowledge and  
27 confidence of opioid misuse, overdose response, and recovery resources increased following the  
28 delivery of a multi-modal interactive substance use disorder curriculum. Community, school, and  
29 student-level multifaceted interventions are needed to prevent reduce NMUPO among adolescents.

30

31 Keywords: opioids, misuse, prevention, pharmacy, adolescent

32 Abbreviations: nonmedical use of prescription opioids (NMUPO), opioid use disorder (OUD), Rx for

33 Addiction and Medication Safety (RAMS)

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42 BACKGROUND

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44 In 2016, 881,000 or 4% of 12-17 year olds in the United States misused opioid pain relievers in the past  
45 year, defined as taking them not as directed, using someone else's prescription, or using them for  
46 reasons other than intended.<sup>1</sup> The most common opioid reported misused was hydrocodone, and the  
47 most common reason reported for misuse was to relieve physical pain. An average of 5% of Rhode  
48 Islanders aged 12 and older reported past year nonmedical use of prescription opioids (NMUPO)  
49 between 2012-2014, the highest in New England.<sup>2,3</sup> While past year NMUPO is prevalent in 12-17 year  
50 olds (5%), it almost doubles in young adults aged 18-25 to 7.6%.<sup>4</sup> In 2017, the percentage of students in  
51 9th grade that reported ever using prescription pain medicine non-medically was 8.9%, 10.6% of males  
52 and 6.3% females.<sup>5</sup> Importantly, these measures are self-reported and subject to social desirability bias,  
53 and thus NMUPO may be underreported by as much as 35% in this population.<sup>6</sup>

54

55 People who misuse opioids frequently obtained opioids from a friend or relative, or were prescribed  
56 them from one doctor.<sup>1</sup> As opioid prescribing dramatically increased among adults and adolescent  
57 family members nationally, prescribing among children and adolescents was infrequent and  
58 unchanging.<sup>7</sup> Still, Miech, et al. reported a 33% increase in the risk of NMUPO among young adults who  
59 were appropriately prescribed an opioid before 12th grade.<sup>8</sup> NMUPO is associated with increasing rates  
60 of emergency room visits, inpatient admissions, transition to subsequent heroin use, increased risk of  
61 HIV and HCV infection, opioid-involved overdose, and death among adolescents.<sup>9-13</sup> The risk of  
62 transition to heroin use is greatest in those that begin NMUPO earlier in adolescence.<sup>14,15</sup>

63

64 Encouragingly, the 2017 "Monitoring the Future," study report, a longitudinal study of secondary school  
65 students' reported use and impressions of drug risk and availability, shows improving trends regarding

66 opioid misuse.<sup>16</sup> 12th graders report the lowest levels of non-heroin opioid use, and 8th, 10th, and 12th  
67 graders report decreasing opioid availability, and increasing or sustained perceived risk and disapproval  
68 of non-medical use of prescription opioids.<sup>16</sup> Even as nonmedical use declines in this population, opioid  
69 use disorder diagnoses have increased,<sup>17</sup> along with opioid overdose deaths, primarily attributed to  
70 heroin and fentanyl.<sup>18</sup> The overall prescription opioid overdose age-adjusted death rate among 15-24  
71 year olds increased from 2% in 2015 to 2.6% in 2016, a 30% annual rate change, while the overall opioid  
72 overdose death rate (including heroin and fentanyl) increased from 7% to 9.3% over the same period, a  
73 32.9% change in rate.<sup>19</sup> The overall societal costs of NMUPO among all ages were estimated to be more  
74 than \$55 billion per year.<sup>20</sup>

75

#### 76 *Risk and Protective Factors*

77

78 Predictors of opioid misuse and use disorder have been identified among adolescents.<sup>21-25</sup> These risk  
79 and protective factors become influential at various times during an adolescents development, and  
80 often relate to physiological changes or psychosocial concerns<sup>23,24,26,27</sup> Categorization of individual,  
81 family, school and community factors are defined by the Office of the United States Surgeon General.<sup>21</sup>  
82 Examples include early initiation of opioid use, mental health problems, peer use, and misperception of  
83 normative use and risk of use for individual factors. Lack of family support and academic success, as  
84 well as, increased availability of opioids are also associated predictors of misuse. Social media use may  
85 also affect substance misuse as heavy use has been associated with higher levels of depression and  
86 anxiety and increased exposure to pro-substance use content that reinforces misuse. (Woods HC et al.  
87 Journal of Adolescence 2016; 51:41-49. Tucker JS et al. J Adoles Health 2013; 53:400-4. Steers et al.  
88 Curr Addict Rep 2016; 3:343-348. AAP Council on Communications and Media. Media Use in School-  
89 Aged Children and Adolescents. Pediatrics 2016; 138: e20162592)

90 For every \$1 invested in youth prevention, researchers observed a \$4 savings in health care costs and \$7  
91 savings in law enforcement and other criminal justice costs.<sup>27</sup> Once a child's NMUPO is diagnosable as  
92 with an opioid use disorder (OUD), less than 25% of adolescents and young adults are offered and  
93 receive evidence-based, medication-first treatment, in part due to healthcare worker stigma.<sup>28,29</sup> While  
94 treatment programs require sustainable funding to ensure adolescents manage their OUD and recover  
95 into adulthood, universal prevention programs have proven patient-, school-, community-level and  
96 economic benefits.<sup>30-32</sup> An example of a universal approach, PROSPER (PROmoting School-community-  
97 university Partnership to Enhance Resilience) model uses school- and family-based prevention  
98 programs. The PROSPER model has observed a decreased in prescription opioid and prescription drug  
99 misuse in adolescents both in the short- and long-term outcomes.<sup>30, 32</sup>

100

101 This study evaluates a student pharmacist-delivered, opioid misuse prevention program developed for  
102 high school students and builds upon previous work for school-based prevention strategies for  
103 adolescents.<sup>33-36</sup> The primary objective of this study was to assess high school students' recall of  
104 knowledge of opioid misuse and awareness of medication safety considerations, including appropriate  
105 use, overdose identification and naloxone administration. Secondly, the study examined the effects  
106 of student substance misuse and its relationship to risk and protective factors. Recognizing predictors of  
107 opioid misuse and use disorder, such as early exposure to opioids, experiencing a safe initial experience  
108 with a psychotropic medication, sibling and/or parent misuse of opioids, parental attention, peer  
109 NMUPO, depression, perceived stress, and academic problems in school, can help direct educational  
110 goals for prevention among this at-risk population.<sup>21,23-25,37</sup>

111

112 METHODS

113

114 The Rx for Addiction and Medication Safety (RAMS) program was a universal, opioid misuse prevention  
115 program developed by University of Rhode Island (URI) College of Pharmacy clinical practice-based  
116 faculty and reviewed and approved by an educational consultant with a Master in Education degree.  
117 The 3-hour curriculum provided 3-4 interactive educational sessions, including a focus on medication  
118 safety (i.e. safe use and storage, proper disposal of opioids), signs and symptoms and risk factors for  
119 opioid misuse and withdrawal, opioid overdose identification and response, and local treatment and  
120 recovery resources for adolescents and their families and friends. The program used role-play, case  
121 scenarios, and the Frayer Model<sup>38</sup> to help guide student learning and knowledge application to real-  
122 world examples. The program was also augmented by social media to reinforce information for high-  
123 school students and faculty, as well as family members who joined the campaign.

124  
125 The RAMS program was piloted with a nonrandomized pre-post study design (Thiese et al.  
126 Observational and interventional study design types; an overview. *Biochem Med (Zagreb)* 2014; 24:199-  
127 210) in 8 Rhode Island public schools among 9<sup>th</sup> grade students. Transition into high school increases  
128 the risk of misuse as freshmen face additional social and psychological challenges, and an environment  
129 with more drug exposure potential.<sup>27</sup> The educational consultant of the program recruited schools over  
130 a 6-month period. Monetary incentives were provided for school participation and additional stipends  
131 were offered for up to 2 high school students to attend a national drug prevention and leadership  
132 summer conference. Prior to program delivery, school committee approval of the curriculum and  
133 corresponding study for all 8 schools was required. Additionally, Rhode Island Department of Education  
134 approval was also needed. Delivery of the program was unique because URI pharmacy students  
135 provided the majority of the curriculum to the schools. Student pharmacists have successfully delivered  
136 a presentation on substance misuse focused on the neuroscience of addiction as a service learning  
137 activity to high school students.<sup>39</sup> The authors noted several advantages of using student pharmacists to



138 deliver the presentation, notably to increase the number of presentations delivered, and to have them  
139 delivered by relatable, typically younger individuals than the researchers. In this study, the  
140 presentations were positively received by both the presenters, the schools, and the students.<sup>39</sup> Student  
141 delivery was decided upon for bolstering educational resources, but also to foster peer relationships  
142 with teens.<sup>40</sup> Before receiving authorization to deliver the curriculum, students volunteered to complete  
143 a faculty-run, train-the-trainer program. The program included adolescent communication and life-skill  
144 development, as well as opioid safety and use disorder, overdose recognition and naloxone  
145 administration, and family/community outreach to prepare for on-school site presentation of the  
146 curriculum.

147  
148 Associated with program participation, 9<sup>th</sup> grade students were invited to complete a confidential,  
149 matched pre- and post-curriculum survey. Parents received opt-out permission forms at least two  
150 weeks prior to survey administration and high-school students were required to assent directly before  
151 completing survey. URI Institutional Review Board approval was also obtained prior to study initiation.  
152 College faculty developed survey to include items on risk and protective factors for substance misuse.  
153 Additional survey items included past nonmedical use of prescription opioids, alcohol and other illicit  
154 drugs, students' perception of risk and/or harm from prescription opioids, and awareness of local and  
155 national treatment and recovery resources. The survey also evaluated for changes in students'  
156 knowledge of proper storage and disposal of prescription drugs, misuse knowledge and addiction  
157 awareness, overdose identification and naloxone administration. Questions used were based on the  
158 2015 Youth Risk Behaviors Survey from the Centers for Disease Control and Prevention<sup>41</sup> and the 2015  
159 Ontario Study Survey from the Canadian Centre for Addiction and Mental Health.<sup>42</sup> A behavioral science  
160 research professor reviewed final survey for methodology and implemented it for administration via  
161 SurveyMonkey®. High school students were provided the survey link and matched by collecting

162 confidential identifiers (i.e. first 3 letters of mother's maiden name, first 2 letters of student's middle  
163 name and day of their birth). Pre-survey administration occurred on the first day of curriculum prior to  
164 delivery and post-survey data was collected at least one month after curriculum conclusion.

165

#### 166 *Statistical Analysis*

167

168 Bivariate analysis was completed separately among pre-intervention survey respondents and the  
169 matched pre-intervention and post intervention survey respondents. Differences between the two  
170 groups of survey respondents (i.e., pre-survey and matched sample) were compared for each variable  
171 using a chi-square test or Fisher's exact test, as appropriate. Bivariate analysis was also completed for  
172 two dichotomous substance use outcome groups during the pre-survey: (1) non-medical use of  
173 prescription pain relief medications in the past 30 days; (2) prescription pain relief, attention-  
174 deficient/hyperactivity disorder and sedative medications, over-the-counter cough medications and/or  
175 loperamide, marijuana and heroin in the previous 30 days. The association of each possible risk factor  
176 with each substance use outcome was evaluated using a chi-square test or Fisher's exact test, as  
177 appropriate. For each of the substance use outcomes, univariate logistic regression was conducted for  
178 each independent variable to determine statistically significant associations with the outcome of  
179 interest. All independent variables with P value <0.20 were included in the adjusted logistic regression  
180 model for each substance use outcome. Diagnostic tests for collinearity were performed between  
181 independent variables and diagnostics of model fit were examined, as guided by Akaike information  
182 criterion and the Hosmer Lemeshow test (David W. Hosmer & Stanley  
183 Lemeshow (2007) Goodness of fit tests for the multiple logistic regression  
184 model, Communications in Statistics - Theory and Methods, 9:10, 1043-  
185 1069, DOI: [10.1080/03610928008827941](https://doi.org/10.1080/03610928008827941)). Based on the adjusted models, the measure of

186 association between outcome and each independent variable was determined by an estimated odds  
187 ratio with a corresponding 95% confidence interval.

188

189 For the matched set of pre/post intervention respondent surveys, change in knowledge from the pre-  
190 intervention survey to the post intervention survey was evaluated using McNemar's test for paired data.

191 For the continuous pre/post scores, each person serves as their own control, allowing for comparisons  
192 across the two groups because all time-invariant confounding is subtracted out by the individual level  
193 differencing and secular trends are less of a concern for this short of a follow-up period. All statistical  
194 tests were two-sided and performed at the 0.05 significance level. All statistical analysis was performed  
195 using SAS 9.4 (Cary, NC.)

196

## 197 RESULTS

198

199 The RAMS program was piloted during the 2016-2017 academic year. There were 969 adolescents who  
200 completed the pre-intervention survey (Table 1). The majority were 14 years old (45%), 52% were male,  
201 and 62% were white. Most (80%) lived in one home only and spoke English at home (82%) and 54%  
202 lived with two parents and siblings. Twenty-four percent reported 5 or more hours of social media use  
203 per day and 22% received mostly C's or lower in school. Forty-seven percent had a mother who  
204 graduated from college and 36% had a father who graduated from college. In their free time, 64%  
205 reported that at least one of their parents always knew where they were. Among those who completed  
206 the pre-intervention survey, 9% reported use of marijuana, 1% reported heroin use, and 7% reported  
207 NMUPO.

208

209 There were 527 adolescents in the matched sample and they were comparable to the pre-survey sample  
210 for the demographic factors in Table 1. The majority were 14 (49%) old, 48% were male, and 70% were  
211 white. Most (80%) lived in one home only and spoke English at home (85%) and 58% lived with two  
212 parents and siblings. Twenty-four percent reported 5 or more hours of social media use per day and 17%  
213 received mostly C's or lower in school. Fifty-two percent had a mother who graduated from college and  
214 39% had a father who graduated from college. In their free time, 68% reported that at least one of their  
215 parents always knew where they were. Among those in the matched sample, 7% reported use of  
216 marijuana, 0% reported heroin use, and 6% reported NMUPO. The matched sample was comparable to  
217 the respondents at the pre-intervention survey, except more were white, and less received mostly C's or  
218 lower.

219

#### 220 *Pre-Post Changes in Substance Misuse Knowledge*

221

222 Among the matched sample of adolescents, there were significant increases in the number of correct  
223 responses reported for opioid misuse knowledge questions (Table 2). From the pre-intervention survey  
224 to the post-intervention survey, significantly more students correctly identified that addiction is a  
225 chronic brain disease (79% to 83%,  $p = 0.05$ ), drug users are not responsible for their addiction (81% to  
226 88%,  $p = 0.003$ ), and drug users do not have weak characters (49% to 57%,  $p = 0.004$ ). The number of  
227 students who correctly identified drug misuse as accepting prescription medications from a friend and  
228 exceeding the recommended dose, increased (70% to 81%,  $p < 0.0001$  and 85% to 88%,  $p = 0.14$ ,  
229 respectively). Finally, there was a significant increase in the number of students who correctly identified  
230 that non-medical use of a prescription medication is defined as use without a prescription (81% to 88%,  
231  $p = 0.001$ ).

232

233 Students were assigned a score for the number of correctly identified opioid withdrawal symptoms  
234 (observed score range, 0 to 12) and steps for managing an opioid overdose (observed score range, -4 to  
235 7; negative values represent only choosing incorrect responses). Students' scores for opioid withdrawal  
236 symptoms increased from 5.9 correct responses (standard deviation (SD) = 3.6) to 6.3 (SD = 3.9;  $p =$   
237 0.04) and scores for identifying the steps to manage an opioid overdose improved from 3.2 correct  
238 responses (SD = 1.7) to 3.9 (SD = 2.3;  $p < 0.0001$ ).

239

240 As knowledge increased, improved confidence was also reported in identifying opioid withdrawal  
241 symptoms (26% to 45%,  $p < 0.0001$ ), identifying signs of an opioid overdose (29% to 46%,  $p < 0.0001$ ),  
242 knowing when to administer naloxone (17% to 45%,  $p < 0.0001$ ) and educating friends and family to  
243 recognize an opioid overdose and safely give naloxone when indicated (27% to 41%,  $p < 0.0001$ ).  
244 Confidence in referral to treatment of friends and family with opioid misuse or use disorder also  
245 improved among 9<sup>th</sup> grade students (31% to 45%,  $p < 0.0001$ ).

246

#### 247 *Predictors of Substance Use at Pre-Survey*

248

249 The prevalence of non-medical use of prescription pain relief drugs, and non-medical use of any drugs  
250 captured in the pre-intervention survey are reported for each level of the demographic factors. These  
251 findings are displayed in Supplementary Table 1.

252

253 At the pre-intervention survey, reports of feeling depressed, under stress, peer use, and perception of  
254 low parental affection increased the odds of NMUPO (Table 3). Adolescents who reported feeling  
255 depressed a little or all the time had over 2 times the odds of reported NMUPO compared to those who  
256 were depressed none of the time, while adolescents who felt stressed or strained had over 5 times the

257 odds of reported NMUPO compared to those that did not feel stressed at all. Reported peer NMUPO in  
258 the past year increased the odds of 9th grade students by 1.9 compared to those who had friends who  
259 did not engage NMUPO. Adolescents who reported their parents showed affection 2 times per year or  
260 less had twice the odds of reported NMUPO, compared to adolescents who reported their parents  
261 showed affection 1-2 times per month.

262

263 At the pre-intervention survey, older age, being under stress, reported illegal drug sale attempts, peer  
264 use of marijuana, and low parental affection were associated with increased odds of non-medical use of  
265 drugs (Table 4). Academic success was reported with decreased odds of non-medical use compared to  
266 earning lower grades (i.e., mostly C's or lower). Adolescents who were 17 years old had five times the  
267 increased odds of non-medical use of drugs compared to 14-year-old peers. Adolescents who felt  
268 stressed or strained had over two times the odds of reported non-medical use of drugs when compared  
269 to those who were not stressed in the last month. Adolescents who reported illegal drug sale attempts  
270 had over three times the odds of reported non-medical use of drugs compared to those who did not  
271 report illegal drug sale attempts. Those surveyed who that reported some to all of their closest friends  
272 used marijuana had twice the odds of reported non-medical use of drugs compared to those that  
273 reported none of their friends were using marijuana. Adolescents who reported their parents showed  
274 affection 2 times per year or less had over twice the odds of reported non-medical use of prescription  
275 pain relief drugs, compared to adolescents who reported their parents showed affection 1-2 times per  
276 month. Grades of C's or lower had 1.5 times the odds of reported non-medical use, where earning A's  
277 decreased the odds by 50% compared to those who received mostly B's.

278

279 DISCUSSION

280

281 The RAMS program provided a universal opioid misuse education program to adolescents uniquely  
282 through its curriculum design and delivery. Freshmen students who participated improved their overall  
283 knowledge of opioid misuse and use disorder (i.e., addiction). Improved knowledge and confidence  
284 were also observed for overdose identification and naloxone administration, as well as increased self-  
285 confidence of knowing when treatment is indicated for a friend or family member and what resources  
286 are available for treatment and recovery.

287

288 Educational prevention programs for teen substance misuse are abundant<sup>21,27,43</sup> though most do not  
289 specifically target opioid misuse.<sup>21,27,43</sup> Programs are usually aimed for students using drug resistance  
290 and general social skills as prevention strategies<sup>27,33</sup> Many others only target risk factors for general  
291 substance misuse or educate specifically on prescription medication safety.<sup>32,43</sup> The RAMS curriculum  
292 provided drug resistance skills through awareness of opioid misuse dangers and situational social skills  
293 by way of role play, but its distinction is its inclusion of content on opioid safety, proper medication  
294 storage and disposal, treatment and recovery support for peers, and overdose recognition and reversal,  
295 including naloxone use. Several states in addition to Rhode Island<sup>43</sup> have proposed or passed substance  
296 use and misuse prevention high school curricula,<sup>45,46</sup> but none have included naloxone education,  
297 despite policies that mandate or recommend naloxone be available in schools<sup>47</sup>. Adolescents can be  
298 successfully trained to administer the one-step intranasal formulation;<sup>48</sup> thus, naloxone education  
299 should be part of prevention curricula. Harm reduction has been effective for alcohol and tobacco  
300 prevention, but related evidence for prescription or illicit drug use has not been studied.<sup>49</sup> A  
301 multifaceted approach, such as RAMS, follows the prevention plan from the Substance Abuse and  
302 Mental Health Services Administration by addressing prescription drug misuse awareness, but  
303 additionally addresses medication safety considerations, harm reduction strategies, and treatment  
304 resources<sup>50</sup> in 9<sup>th</sup> grade students.

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Seven and six percent of adolescents who completed the pre-intervention and matched survey, respectively, reported NMUPO. Use among the study population corresponds with the 2017 self-reported data from Rhode Island of 8.9% NMUPO among 9<sup>th</sup> grade students.<sup>5</sup> Of those adolescents that state NMUPO, their associated risks were depression, stress, peer use, and perception of low parental affection. Additional studies have observed similar mental health risk factors for NMUPO.<sup>23-25</sup> Though self-medication for physical pain is the most common reason for misuse<sup>1</sup>, motives to self-treat depression and anxiety (i.e., emotional pain) have been observed in adolescents.<sup>23,24,51</sup> Peer use and perception of low parental support both have been reported as known risks for NMUPO.<sup>21,37</sup> Risks associated with overall substance misuse, including prescription opioids in the pre-intervention group were older age, lack of academic success, being approached to purchase drugs, as well as stress, peer use and lack of parental affection. School-risk factors, such as academic failure as early as late elementary school, and community-risk factors of ease of drug access have both been observed in other studies and are risks defined by the Surgeon General.<sup>21,37</sup> Age, it seems, may be a reflection of the early initiation of substance use, given the increasing odds with each year of age.<sup>21</sup> RAMS curriculum currently focuses on peer use and drug access through normative education, misuse awareness, and proper storage and disposal. A potential expansion is to further the discussion of self-medication risks and stress reduction strategies as outcomes indicate stress management and mental health resources may be warranted for schools. The perceived lack of support among adolescents in the study highlights the need for family-centered prevention strategies in addition to a school-based approach.<sup>32,35</sup> Parental involvement is essential for prevention strategies though parents and caregivers are difficult to recruit and retain in such programs.<sup>21,52</sup> Use of social media may be a novel approach to reach and connect parents and teens; however, evidence is needed on its effectiveness.



329 RAMS is delivered in several short, active-learning sessions with student pharmacists within the  
330 classroom, modified to fit the pilot school's schedule. This approach allows for pharmacy students to  
331 enhance the discussion and knowledge recall among adolescents as they are serving as peer instructors.  
332 Student pharmacists also provided advanced knowledge of prescription opioids, overdose education,  
333 including naloxone, which is in contrast to National Institute on Drug Abuse teen program that simply  
334 use online materials to serve as teacher facilitator guides.<sup>50,53</sup> This is the first work to demonstrate  
335 comprehensive opioid misuse prevention education in a school-setting using pharmacy students.  
336 However, student pharmacists have provided opioid safety and overdose prevention to emergency  
337 department patients, and this program was found to be both feasible and improve patients knowledge  
338 of opioids.<sup>54</sup> Prevention education by student pharmacists in a school-setting through the RAMS  
339 program is achievable, improves knowledge of opioid misuse and its risks, and enhances students'  
340 confidence to engagement in harm reduction strategies and support family and friends in treatment and  
341 recovery of opioid use disorder.

342

#### 343 *Limitations*

344

345 Development of the opioid misuse curriculum was based on clinical faculty expertise and evidence-  
346 based literature supporting the need for education on opioid misuse and increasing awareness of its  
347 risks and consequences, as well as safe use of opioids, proper medication storage and disposal, harm  
348 reduction strategies and treatment support.<sup>50,55</sup> Therefore, our curriculum was not matched to a  
349 standard and may possess features not tailored to adolescent education. Though in its design, the  
350 curriculum does provide drug resistance skills and normative education to students while additionally  
351 providing harm reduction strategies to help enhance competence skills training.

352

353 Delivery of the curriculum proved to be difficult at times. Pharmacy student recruitment for the train-  
354 the-trainer program was robust; however, continued interest and motivation of pharmacy students to  
355 participate in more than 1 or 2 classroom sessions was limited. Steps to enhance pharmacy student  
356 participation has been implementation for subsequent curriculum delivery in the form of student  
357 professional development funds. Conversely, pharmacy students were unprepared for occasional  
358 behavioral issues within the classroom among high-school students. Incentives provided to high schools  
359 were to be set aside to offset costs of having teachers present for classroom management and  
360 discipline. However, some pharmacy students found classroom management of adolescents challenging  
361 and an obstacle to facilitating discussion of the program key elements. Additional limitations include  
362 miscommunication of high school administration and staff which led to conflicts in delivery and timing of  
363 the curriculum, necessitating shortened duration of sessions and rescheduled sessions. Certain schools  
364 also had different classroom needs, such as auditorium-style delivery, advisory times and rotating  
365 schedules adding to the challenge of presenting curriculum as an interactive program. Challenges of  
366 existing school culture when implementing a novel curriculum is expected. As the RAMS program  
367 continues within schools, scheduling and communication issues hopefully will subside as curriculum  
368 expectations will be known be all parties.

369

370 Data collection also presented implementation challenges. Surveys were tested for length prior to  
371 administration and found to be 10- to 15-minute duration. Thus, pre-surveys were originally scheduled  
372 to be administered directly prior to the opening curriculum session. However, some high school  
373 students took upwards of 45-60 minutes to complete the survey and arrangements had to be made to  
374 reschedule subsequent sessions. In addition, youth had trouble with the confidential identifiers,  
375 particularly mother's maiden name. Therefore, the number of matched results were significantly  
376 reduced based on student understanding of the identifiers, as students and faculty were unprepared to

377 explain what we assumed was common knowledge. A new process for matched data collection will be  
378 implemented going forward with the removal of mother's maiden name and replaced by street name  
379 where they reside. Post surveys were to be administered 1-2 months after curriculum intervention.  
380 Nevertheless, some schools scheduled post surveys several months after curriculum, thus recall bias  
381 may be relevant due to different timing of the administration for post results.

382

383 The responses to the survey were self-report and subject to reporting bias. In addition, based on the  
384 self-reported data, adolescents' substance use and knowledge could be misclassified.<sup>6</sup> The matched  
385 adolescents may not be representative of the study sample; thus, our results are subject to selection  
386 bias. In addition, secular trends may be present that our current approach did not consider, and our  
387 analyses could be subject to unmeasured confounding. The results from baseline are cross-sectional, so  
388 temporal sequence and causality are not possible to establish. Future longitudinal studies evaluating risk  
389 factors and subsequent opioid use initiation are warranted. In these studies, the intervention could be  
390 randomized to eliminate unmeasured confounding. Our pilot project evaluated this training among high  
391 school students in Rhode Island and these results may not be generalizable to a broader population  
392 without additional considerations.

393

394 Future goals are to create a video booster curriculum to sustain knowledge gained and evaluate the  
395 disseminated or spillover effects of the RAMS training among high school students. We plan to evaluate  
396 this program in additional Rhode Island schools to address gaps in opioid misuse prevention education  
397 in the state. Further goals are to evaluate the longitudinal effect of prescription opioid misuse, measure  
398 the prevalence of heroin and other substance use among adolescents, with the objective to observe a  
399 decrease in use as a result of increased knowledge of opioid misuse, its risks, and treatment of opioid  
400 use disorder. Additionally, we are creating a corresponding RAMS website for high school teachers and

401 students, as well as parents and caregivers to expand upon the social media campaign. The website will  
402 have video curriculum and additional teacher and parent resources to enhance recruitment and  
403 participation in prevention strategies.

404

#### 405 CONCLUSIONS

406

407 Among adolescents surveyed the lifetime prevalence of NMUPO was 6%-7%. NMUPO was associated  
408 with mental health problems, peer use and perceived lack of parental affection. Students receiving  
409 multi-modal prevention education for prescription opioid misuse increased their knowledge and  
410 confidence in understanding of opioid misuse, overdose identification and its response, and recovery  
411 resources. Inclusion of harm reduction strategies delivered by student pharmacists is a novel approach  
412 to prevention education. Further evidence is needed to ensure the curricula decreases NMUPO and  
413 whether interventions for stress management and mental health, as well as family-centered strategies  
414 should be incorporated into the universal-school based program.

415

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417

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