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4 **Impact of pharmacist provision of naloxone at an independent community pharmacy**
5 **operating under state naloxone protocol**

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28 Lynn Connelly is the owner of Medicine Mart Pharmacy. Medicine Mart Pharmacy is an active
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42 **ABSTRACT:**

43 Objectives: The primary objective of this study was to determine if a universal offer to provide
44 naloxone to all patients dispensed an opioid, accompanied by patient counseling, increases
45 naloxone possession rates among patients of an independent community pharmacy.

46

47 Methods: This study was conducted at an independent community pharmacy over a 4-month
48 period. Patients 18 years of age or older who presented a prescription for an opioid medication
49 were included in the study. Any patient with a known allergy to naloxone was excluded from
50 the study. The pharmacist provided counseling and dispensed naloxone pursuant to state
51 protocol upon patient request. Deidentified data from the study period was matched to data
52 from the previous year, prior to the initiation of the naloxone service, to determine if
53 community pharmacy-based naloxone dispensing by protocol improved the naloxone
54 medication possession ratio (MPR). Factors associated with increased risk of opioid-related
55 overdose were collected to identify the most common risk factors among patients dispensed
56 naloxone. Descriptive statistics were used to report data regarding factors associated with
57 increased risk of opioid-related overdose for patients dispensed naloxone.

58

59 Results: Following the introduction of a pharmacist driven naloxone dispensing service at an
60 independent community pharmacy, the naloxone MPR doubled from 1.6% to 3.2%. Of the nine
61 patients dispensed naloxone during the study period, 87.5% presented with ≥ 2 risk factors for
62 increased risk for opioid related overdose. The most common risk factors identified were high
63 opioid dose (>50 MME) and concomitant benzodiazepine use.

64

65 Conclusions: Community pharmacy-based naloxone dispensing provides access to naloxone.
66 Upon implementation of a naloxone dispensing service, there was an increase in MPR and total
67 number of naloxone doses dispensed. A similar service could potentially be implemented in
68 other states as scope of practice and state law allows.

69

70 **Introduction (318)**

71 Reducing the number of opioid associated deaths remains a public health priority. In
72 2017, prescription opioids alone accounted for more than 47,000 deaths in the United States.¹
73 The Surgeon General of the United States cites a surge in illicitly manufactured synthetic
74 opioids as a contributing factor in the rapid increase in number of overdose deaths between
75 2010 and 2016.² The CDC recommends that naloxone be considered for all patients receiving
76 more than 50 morphine milliequivalents (MME) per day.¹

77

78 While all 50 states have laws that expand access to the reversal agent through
79 pharmacy dispensing, in 2018 naloxone was provided to only 1 in 69 patients dispensed a high
dose opioid. Pharmacists are uniquely positioned to provide the public with access to naloxone

80 and promote education for safe use of opioid analgesics.³ As an increasing number of patients
81 receive high dose opioids for management of chronic pain, pharmacists can play an important
82 role in addressing the opioid epidemic by utilizing the prescription drug monitoring program
83 (PDMP), identifying patients who are at a higher risk for overdose, and dispensing naloxone.²

84 Various strategies have been implemented to improve the availability and use of
85 naloxone. One study conducted at the state level demonstrated a significant increase in the
86 rate of naloxone dispensing per 100,000 people following the enactment of co-prescription
87 mandates in Virginia and Vermont. Naloxone co-prescription does not account for patient
88 diagnoses or additional risk factors, nor does it expand access to patients at risk of experiencing
89 an opioid overdose related to illicitly manufactured opioids.⁴ While naloxone may be prescribed
90 to a patient, it may not be accessible. A survey of pharmacies in a metropolitan area
91 demonstrated that intranasal naloxone was available in 34% of pharmacies, and more likely to
92 be available from a chain pharmacy than an independent pharmacy.⁵ The purpose of this study
93 is to evaluate the potential impact of a naloxone dispensing service at an independent
94 community pharmacy.

95

96 **Objectives (67)**

97 The primary objective of this study was to determine if a universal offer to provide
98 naloxone to all patients dispensed an opioid accompanied by patient counseling improves
99 naloxone possession rates among patients of an independent community pharmacy.

100 The secondary objective of this study was to identify factors associated with increased
101 risk of opioid-related overdose that may be common among patients dispensed naloxone at an
102 independent community pharmacy.

103

104 **Methods (340)**

105 This study was a single-site data review at an independent community pharmacy
106 granted exemption by the University of South Carolina Institutional Review Board Committee.
107 Any patient 18 years of age or older who presented a prescription for an opioid medication
108 between November 1, 2019 and February 28, 2020 was included in the study. Any patient with
109 a known allergy to naloxone was excluded from the study. When a new prescription for an
110 opioid medication was presented, pharmacists offered to provide information about the
111 benefits of naloxone to the patient. Upon pharmacist counseling and subsequent offer to
112 provide naloxone, pharmacists dispensed naloxone to patients pursuant to The South Carolina
113 Board of Medical Examiners and The South Carolina Board of Pharmacy's Joint Protocol to
114 Initiate the Dispensing of Naloxone HCl Without a Prescription, hereafter referred to as the
115 joint protocol.⁶ Interventions resulting in the dispensation of naloxone were documented
116 utilizing an electronic care (eCare) plan.

117 Deidentified data from the study period was matched to a control period from the
118 previous year (November 1, 2018 to February 28, 2019) prior to the initiation of the naloxone
119 service to determine if community pharmacy-based naloxone dispensing under the joint
120 protocol improved the naloxone possession rate among patients dispensed opioid medications.
121 The naloxone medication possession rate (MPR) was expressed as the percentage of patients
122 dispensed an opioid prescription who also received naloxone. The study period MPR was
123 compared to the MPR from the control period to determine if targeted intervention by
124 community pharmacists impacted medication possession rates. Prescriber designation (MD,
125 DO, NP, PA, RPh) was evaluated for each naloxone prescription dispensed. For patients
126 dispensed naloxone, the number of daily morphine milliequivalents (MME) dispensed to the
127 patient and identified factors associated with increased risk of opioid-related respiratory
128 depression were recorded. Risk factors recorded included concomitant use of benzodiazepine,
129 sedative/hypnotic, muscle relaxant, short acting bronchodilator, long acting bronchodilator,
130 montelukast, roflumilast, or anti-retroviral therapy.

131 Descriptive statistics were used to report data regarding factors associated with
132 increased risk of opioid-related overdose for patients dispensed naloxone by an independent
133 community pharmacy.

134

135 **Results (216)**

136 During the study period, 251 unique patients were dispensed an opioid prescription.
137 Eight of these patients were dispensed naloxone. The average age of the patients was $49.4 \pm$
138 4.8 years old (mean \pm SEM; median=54); 87.5% were male. Patients were dispensed an average
139 of 115.8 ± 38 MME per day (median=60).

140 Following the introduction of a pharmacist driven naloxone dispensing service at an
141 independent community pharmacy, the naloxone MPR doubled. During the study period, 3.2%
142 of patients dispensed an opioid prescription received naloxone compared to 1.6% of patients
143 during the control period (Table 1). All patients dispensed naloxone under the state's joint
144 protocol were dispensed the naloxone prefilled nasal spray (4 mg/0.1 mL).
145 Most patients (87.5%) had two or more risk factors for opioid related overdose. The most
146 common risk factors identified were high dose opioid prescription and concomitant
147 prescription benzodiazepine use (Figure 1). Risk factors with zero patients presenting are not
148 shown.

149 During the study period, nine total doses of naloxone were dispensed to eight unique
150 patients. Pharmacists dispensed 44% of doses under the joint protocol without a prescription
151 order; the remaining 56% of doses were written by a medical doctor (MD) or doctor of
152 osteopathy (DO). During the control period, three doses of naloxone were dispensed, and all
153 doses were co-prescribed by an MD.

154

155 **Discussion (782)**

156 During this study, there was an increase in both the total number of doses of naloxone
157 dispensed and naloxone MPR. Half of the patients who received naloxone during the study
158 period were provided naloxone by a pharmacist. Of note, one patient was dispensed 2
159 prescriptions for naloxone during the study period, both originating from a physician. An
160 increased awareness and focus on safe use of opioids by the pharmacy staff following the
161 initiation of the naloxone service may have had a positive impact on the number prescriptions
162 written by a physician that were ultimately filled for the patient. Differences in naloxone
163 prescribing rates from physicians and mid-level providers between the intervention and control
164 periods were not assessed as part of this study. Prescriptions for naloxone that were profiled
165 (prescribed but never dispensed) were not accounted for as part of this study and may have
166 differed between the control and study period.

167 Four naloxone products are available to patients under the joint protocol—prefilled
168 naloxone nasal spray (4 mg/0.1 mL), intramuscular naloxone (1 mg/mL) with mucosal atomizing
169 device (MAD), naloxone for intramuscular injection (0.4 mg/mL), and naloxone auto-injector (2
170 mg/0.4 mL). Three of the four possible formulations of naloxone were available to patients
171 during the study period; the naloxone auto-injector was not available through the pharmacy's
172 naloxone dispensing service. All patients included in the study received intranasal naloxone as a
173 prefilled device. Factors that may contribute to product selection include availability, cost,
174 manual dexterity, and patient preference.

175 Because all patients with an opioid prescription are eligible candidates for naloxone
176 under the state's joint protocol, patients prescribed fewer than 50 MME per day were not
177 excluded from this study. In this study, 3.2% of patients dispensed an opioid prescription
178 received naloxone. This is higher than the last known national rate for naloxone dispensing, 1 in
179 69 patients or 1.4%. This figure included only patients prescribed a high dose opioid (>50 MME
180 per day) and is not directly comparable to the MPR determined in this study.³

181 Most patients dispensed naloxone had more than 1 risk factor for opioid related
182 overdose, with the most common risk factors being high dose opioid prescriptions and
183 benzodiazepine use. The risk factors evaluated as part of this study are not all inclusive.
184 Concomitant use of prescription medications was utilized as a marker for a subset of risk factors
185 that may predispose patients to an unintentional opioid related overdose cited in other reports
186 or mentioned in the state's joint protocol.^{5,6}

187 This study supports conclusions of other studies evaluating pharmacy-based naloxone
188 dispensing. While no such study is available for South Carolina patients, a large-scale study
189 assessing naloxone dispensing rates for Ohio Medicaid patients demonstrated the significant
190 impact of pharmacists dispensing naloxone under Ohio's state naloxone dispensing protocol.
191 Statewide naloxone dispensing rates were 24 times greater (a 2328% increase) following the

192 passage of expanded naloxone access laws. Among the Ohio Medicaid population, the mean
193 number of naloxone orders increased from 0.025% pre-protocol to 6.09% post-protocol.⁸

194 Increasing awareness of naloxone availability with sensitivity to patient perception
195 provides a challenge. Many states, including South Carolina, have a public list of pharmacies
196 that carry naloxone. Unfortunately, inclusion on such lists is not indicative of naloxone
197 availability. In a survey of pharmacies listed in one such directory in North Carolina, 39.1% of
198 listed pharmacies did not have naloxone in stock. Independent pharmacies were less likely to
199 stock naloxone than chain pharmacies (OR=0.12, 95% CI 0.06-0.25).⁹ Patients who may benefit
200 from naloxone may be unaware that naloxone is an available resource and that it may be
201 purchased without a prescription in many states. Although the total number of doses of
202 naloxone dispensed is low, provision of naloxone at the independent community pharmacy did
203 increase availability.

204 Misconceptions surrounding the availability and utility of naloxone must be addressed
205 to expand naloxone provision.^{10,11} Patient and pharmacy employee perceptions were not
206 objectively assessed as part of the study. Additional research is warranted to assess patient and
207 pharmacist perceptions of pharmacy driven naloxone dispensing services. Misinformation
208 regarding naloxone availability could potentially impact access. A lack of formal training may
209 limit the effectiveness of a pharmacy-based naloxone dispensing service.

210 At the time this study was completed, the pharmacy was also a participant in the Flip
211 the Pharmacy initiative, which focuses on sustainable, scalable innovation in pharmacy practice.
212 This study was completed ahead of the Flip the Pharmacy opioid progression which focuses on
213 safe utilization of opioid analgesics. As part of this progression, pharmacy staff are provided
214 formal training to integrate opioid safety interventions, including the offer to provide naloxone,
215 into the pharmacy's workflow. Completion of the opioid change package progression provides
216 an opportunity for application and amplification of the service evaluated in this study.

217

218 **Limitations (104)**

219 The study is limited by its small sample size. More robust data regarding naloxone
220 possession rates would be valuable in assessing the impact of independent community
221 pharmacy-based naloxone services.

222 The results of this study may not be generalizable to a broader population. All patients
223 who received naloxone during the study period were white and carried third-party insurance
224 that covered naloxone. Anecdotally, cost was not cited by any patient as the reason for
225 declining discussion about or provision of naloxone. While a similar service could be
226 implemented at other independent community pharmacies, patient eligibility may differ as
227 expanded access laws vary from state to state.

228

229 **Conclusions (64)**

230 Community pharmacy-based naloxone dispensing provides access to naloxone. Upon
231 implementation of a naloxone dispensing service, there was a modest increase in total number
232 of naloxone doses dispensed and MPR. A similar service could potentially be implemented in
233 other states as scope of practice and state law allows. Additional research is needed to
234 determine the best method for increasing the number of naloxone doses dispensed.

235

236 Citations (References)

- 237 1. Dowell D, Haegerich TM, Chou R. CDC guideline for prescribing opioids for chronic
238 pain—United States 2016. *JAMA*. 2016;315(15):1624-1645.
- 239 2. Office of the Surgeon General. U.S. Surgeon General’s advisory on naloxone and opioid
240 overdose. [https://www.hhs.gov/surgeongeneral/priorities/opioids-and-](https://www.hhs.gov/surgeongeneral/priorities/opioids-and-addiction/naloxone-advisory/index.html)
241 [addiction/naloxone-advisory/index.html](https://www.hhs.gov/surgeongeneral/priorities/opioids-and-addiction/naloxone-advisory/index.html). Update April 5, 2018. Accessed March 27,
242 2020.
- 243 3. Guy GP, Haegerich TM, Evans ME, Losby JL, Young R, Jones CM. Vital Signs: Pharmacy-
244 Based Naloxone Dispensing — United States, 2012–2018. *MMWR Morb Mortal Wkly*
245 *Rep*. 2019;68(31):679-686. doi:10.15585/mmwr.mm6831e1
- 246 4. Sohn M, Talbert JC, Huan Z, Lofwall MR, Freeman PR. Association of naloxone
247 coprescription laws with naloxone prescription in the United States. *JAMA Network*
248 *Open*. 2019;2(2):e196215.
- 249 5. Guadamuz JS, Alexander GC, Chaudhri T, Trotzky-Sirr R, Qato DM. Availability and Cost
250 of Naloxone Nasal Spray at Pharmacies in Philadelphia, Pennsylvania, 2017. *JAMA Netw*
251 *Open*. 2019;2(6):e195388. doi:10.1001/jamanetworkopen.2019.5388
- 252 6. Gardner SR, Russell CS. The South Carolina Board of Medical Examiners and The South
253 Carolina Board of Pharmacy’s Joint Protocol to Initiate the Dispensing of Naloxone HCl
254 Without a Prescription. [http://naloxonesavessc.org/wp-](http://naloxonesavessc.org/wp-content/uploads/2018/11/Joint_Naloxone_Protocol.pdf)
255 [content/uploads/2018/11/Joint_Naloxone_Protocol.pdf](http://naloxonesavessc.org/wp-content/uploads/2018/11/Joint_Naloxone_Protocol.pdf). November 17, 2016. Accessed
256 August 18, 2018.
- 257 7. Horsfall JT, Sprague JE. The Pharmacology and toxicology of the ‘Holy Trinity’. *Basic Clin*
258 *Pharmacol Toxicol*. 2017;120(2):115-119.
- 259 8. Gangal NS, Hincapie, AL, Jandarov R, et al. Association between a state law allowing
260 pharmacists to dispense naloxone without a prescription and naloxone dispensing rates.
261 *JAMA Network Open*. 2020;3(1):e1920310.
- 262 9. Egan KL, Foster SE, Knudsen AN, Lee JGL. Naloxone availability in pharmacies and
263 neighborhood inequities in access. *Am J Prev Med*. 2020;58(5):699-702.
- 264 10. Kurian S, Baloy B, Baird J, et al. Attitudes and perceptions of naloxone dispensing among
265 a sample of Massachusetts community pharmacy technicians. *J Am Pharm Assoc(2003)*.
266 2019;59(2019):824-831.

267 11. Green TC, Case P, Fiske H, et al. Perpetuating stigma or reducing risk? Perspectives from
268 naloxone consumers and pharmacists on pharmacy-based naloxone in 2 states. *J Am*
269 *Pharm Assoc*(2003). 2017;57(2):S19-S27.e4.