# Identifying Injection Drug Users at Risk of Nonfatal Overdose

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### **Abstract**

*Objectives*: Drug overdose is the second leading cause of accidental deaths among U.S. adults aged 15–64 years. Emergency physicians have a unique opportunity to provide overdose prevention interventions, because habitual drug users are in frequent need of medical care. The authors evaluated associations between individual-level risk factors and experiencing an overdose in the past six months to determine which characteristics and behaviors may be most predictive of overdose.

*Methods:* The authors used data from a sample of street-recruited habitual drug users who participated in face-to-face interviews about overdose from November 2001 to February 2004. This analysis was restricted to 772 respondents who had been injecting for at least one year and who had injected heroin within the past two months.

**Results:** A total of 16.6% of participants had overdosed in the past six months. Characteristics and behaviors that were independently associated with an increased risk of a recent overdose were having had a prior overdose (odds ratio [OR], 28.58; 95% confidence interval [CI] = 14.10 to 57.96), using cocaine/crack in the past six months (OR, 2.07; 95% CI = 1.25 to 3.45), using alcohol in the past six months (OR, 1.90; 95% CI = 1.01 to 3.57), experiencing serious withdrawal symptoms in the past two months (OR, 2.70; 95% CI = 1.58 to 4.61), and younger age.

**Conclusions:** Drug users who have previously experienced a nonfatal overdose are at very high risk of experiencing future overdoses. Further longitudinal studies are needed to identify robust predictors of overdose risk over time in habitual drug users, but these data suggest that drug users who have overdosed warrant aggressive prevention efforts such as agonist maintenance treatment or provision of take-home naloxone.

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verdose is the second leading cause of accidental death among U.S. adults aged 15–64 years<sup>1</sup> and the leading cause of death among drug users.<sup>2</sup> Death rates from overdose have continued to climb in many regions, <sup>1,3</sup> and more than two thirds of drug users report at least one nonfatal overdose in their lifetime.<sup>4</sup> There were more than two million drug-related emer-

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gency department visits in 2004,<sup>5</sup> and nonfatal overdose is associated with substantial morbidity (e.g., physical injuries, aspiration-related lung injury and infections, seizures, and peripheral neuropathy).<sup>6</sup>

Demographic, health, and drug use characteristics and risk behaviors are associated with an increased risk of overdose. Indicators of social marginalization, including homelessness,<sup>7,8</sup> Axis I and II mental health disorders and feelings of hopelessness, 9-11 and antisocial behavior, 12 have been associated with drug overdose. Overdose death is more likely following human immunodeficiency virus (HIV) seroconversion and among those with abnormal liver function, shortness of breath, and diarrhea, 13 suggesting that common mechanisms of overdose death (respiratory depression and cardiac arrest)<sup>14</sup> may be more likely in individuals with systemic comorbidities. Length of drug use, <sup>4,15</sup> polydrug use, <sup>4,16–18</sup> risky drug use, <sup>13,15,19</sup> disrupted life circumstances, <sup>20,21</sup> and conflicts within social networks<sup>19</sup> are associated with overdose. Risk of overdose increases with periods of reduced tolerance, including release from prison<sup>22</sup> and naltrexone detoxification, 23 while overdose risk is decreased with agonist maintenance therapy<sup>24</sup>; opioid metabolites in the hair of overdose decedents are far below the levels of active heroin users,<sup>25,26</sup> suggesting periods of abstinence preceding death. Drug dependence may have a more complicated relationship with overdose, with heroin dependence possibly protecting users through increased tolerance and cocaine dependence resulting in direct toxicity.<sup>27</sup> Few studies have looked at the breadth of potential risk factors together in one sample of habitual drug users while also controlling for history of overdose, which may be an important predictor of future overdose.<sup>24,28</sup>

Interventions for opioid overdose prevention include expanded access to opioid agonist maintenance treatment, training in rescue breathing, and prescription of take-home naloxone, the latter of which has been adopted by numerous departments of health and a growing number of medical providers. <sup>29–31</sup> To help physicians target patients in need of overdose prevention messages, we evaluated the associations between a variety of individual-level characteristics and behaviors hypothesized to be related to overdose risk and developed a model predictive of recent overdose.

#### **METHODS**

#### Study Design

A cross-sectional study was conducted among current drug users to assess risk factors for recent overdose. The institutional review board at the New York Academy of Medicine approved the study, and all study subjects provided written consent at the time of the interview.

## **Study Setting and Population**

Participants were recruited through targeted outreach techniques (described elsewhere)<sup>32,33</sup> from selected neighborhoods in a large urban area in the United States with high proportions of minority populations from November 2001 to February 2004. Eligibility requirements included participants being 18 years of age or older and having used heroin, crack, or cocaine at least once in the two months before the interview.

## Study Protocol

Structured in-person interviews were conducted in English or Spanish by trained interviewers at two stationary storefronts in central Harlem (Manhattan) and the South Bronx. Identifying information was collected from participants to ensure that individuals did not participate more than once in the study, but this information was kept separate from responses to the questionnaire to ensure anonymity, linked only by a unique identification number and stored in separate files. Data were entered and maintained electronically.

#### Measures

We assessed demographic characteristics (gender, age, race/ethnicity, marital status, educational attainment, and homelessness in the past six months), health status, drug use, and risk behaviors previously shown to impact overdose risk.

*Overdose Experience*. Consistent with investigations in Adelaide, Australia, <sup>17</sup> and San Francisco, California, <sup>18</sup>

overdose was defined as "someone who collapses, has blue skin color, convulsions, difficulty breathing, loses consciousness, cannot be woken up, or has a heart attack or dies while using drugs." Respondents were asked if they had ever overdosed during their lifetime; those who had overdosed were asked how many times they had overdosed in the past six months, in the past year, and in their lifetime. For the purposes of this analysis, a recent overdose was defined as experiencing at least one overdose within the past six months, whereas a prior overdose was defined as experiencing at least one overdose prior to the past six months. We also asked participants if they had ever seen someone else overdose and if they had ever personally known anyone who died of a drug overdose.

Health Status. Respondents were asked to rate their overall health; responses of excellent, very good, and good were grouped together, while responses of fair and poor were grouped together to create a more clear contrast between those with better and worse self-rated health. Respondents were also asked to report their HIV status (positive, negative, or unknown). Additionally, the Medical Outcomes Survey Short-Form 36 (SF-36) was used to assess health-related quality of life. Summary scores were created for eight distinct components: physical functioning, role limitations due to physical problems, role limitations due to emotional problems, social functioning, bodily pain, vitality, general health, and mental health. Each measure was scored on a scale from 0 to 100, with higher scores indicating better health. These component scores have been repeatedly validated34-36 and have been successfully applied to drug users in other studies.37

**Drug Use and Risk Behaviors.** Length of drug-using career was calculated from the participants' age of first use and last use of drugs. We also assessed the use of specific drugs in the past six months, including heroin, cocaine or crack, alcohol, and tranquilizers or benzodiazepines, and the number of types of drugs used in the past six months (marijuana, heroin, crack, cocaine, alcohol, cigarettes, methamphetamines, tranquilizers or barbiturates, hallucinogens, or other drugs). The number of types of drugs used in the past six months was categorized into two groups  $(1-5, \geq 6)$  to differentiate between those who had and had not used more than the sample mean number of types of drugs.

Participants were asked about any risky practices they had engaged in at their last injection, including splitting drugs with someone else using a needle or sharing a cooker, cotton, rinse water, or needle with someone else. We also asked if participants had ever used a syringe exchange program. Finally, we asked about sexual risk behaviors in the past two months, including having a sexual partner with hepatitis, giving or receiving drugs or money for sex, using condoms less than 80% of the time with casual partners, or having more than the sample median number of sexual partners (>1).

We assessed heroin and cocaine dependence using the Severity of Dependence Scale (SDS), a valid and reliable measure that assesses the degree of psychological dependence experienced by users of different types of illicit

drugs in different settings. 38,39 The SDS consists of five items: 1) "How often did you think your use of [named drug] was out of control?," 2) "How often did the prospect of going without [named drug] make you very anxious or worried?," 3) "How much did you worry about your [named drug] use?," 4) "How often did you wish you could stop?," and 5) "How difficult would you find it to stop or go without [named drug]?." Each item was scored on a four-point scale (for items 1-4: 0 = never/ almost never. 1 = sometimes. 2 = often. 3 = always/nearly always; for item 5: 0 = not difficult, 1 = quite difficult, 2 = quite difficultvery difficult, 3 = impossible). The total SDS score was obtained by adding the scores of all items (range, 0–15), with higher total scores indicating higher levels of dependence. A test of the internal consistency of the scale among five samples demonstrated Cronbach's α values between 0.80 and 0.90 and correlation levels between total scores and factor scores >0.99.38 The SDS can be adapted to cover different types of drugs and different time periods by modifying the reference to the named drug and the specified time frame; we assessed heroin and cocaine dependence in the past year. A study reporting on the psychometric properties of the SDS in samples of heroin users showed that total SDS scores  $\geq 7$  were generally indicative of severe heroin dependence. 17,38,40 Another study of recent cocaine users showed that a total SDS score of  $\geq 3$  discriminated best between the presence and absence of a Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV) diagnosis of cocaine dependence. 41 Consistent with these findings, we considered scores  $\geq 7$  and  $\geq 3$  as indicative of dependence on heroin and cocaine, respectively.

Serious withdrawal symptoms in the past two months were also assessed; examples of serious withdrawal symptoms provided to participants included stomach cramps, diarrhea, vomiting, and sweating. Finally, we asked about participation in drug treatment during the past six months, including methadone maintenance, detoxification, and other drug treatment programs including Narcotics Anonymous and therapeutic communities.

# **Data Analysis**

This analysis was restricted to participants who reported a drug injection career of at least one year and who had injected heroin in the past two months to assess determinants of recent overdose among long-term habitual drug users rather than new or less frequent users. We restricted the analysis to heroin users to facilitate comparisons with other studies. We described the demographic characteristics, health status, drug use and risk behaviors, and overdose experience of the participants. We calculated the prevalence of recent overdose and compared characteristics of those who had and had not experienced a recent overdose. Finally, we created a multivariable logistic regression model, including all variables that significantly improved model fit using log likelihood ratio tests to build the best model predictive of recent overdose. The predictive ability of the model was assessed using the c-statistic, which corresponds to the area under the receiver operating characteristic curve. 42 Higher values of the c-statistic indicate better predictive ability, with a value of 0.5 indicating no predictive ability and a value of 1.0 indicating perfect predictive ability. 43 All measures described here and listed in Table 1 were considered as potential covariates for the multivariable model. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated for all variables in the multivariable model. All analyses were performed with the SAS version 8.01 software package (SAS Institute, Inc., Cary, NC).

#### **RESULTS**

We analyzed data from 772 participants who had injected for at least one year and who had injected heroin within the past two months. Most respondents were male, 25–44 years of age, Hispanic, and unmarried, and about half had less than a high school education (Table 1). The majority reported their general health to be fair or poor; 11.5% were HIV positive, and 12.6% did not know their HIV status. Most had been using drugs for more than ten years, had used cocaine or crack and alcohol in the past six months, and reported using six or more types of drugs in the past six months. Just less than half reported at least one risky injection practice at their last injection, nearly 60% had used a needle exchange program, and about half reported risky sex in the past two months. The majority of participants were severely dependent on heroin and on cocaine, and more than one third had experienced serious withdrawal symptoms in the past two months. A history of drug treatment was common, with about 40% reporting methadone maintenance and 61% reporting detoxification in the past six months. More than two thirds of participants had ever witnessed an overdose and had personally known someone who died of an overdose.

Overall, 16.6% of respondents had experienced an overdose in the past six months (Table 1). A greater proportion of those who recently overdosed than those who did not were male, younger, and recently homeless. Recent overdose was also associated with poorer selfreported health and limitations due to physical and emotional problems, social functioning, pain, general and mental health, and use of other drugs in addition to heroin during the past six months. Those with a recent overdose were also more likely to have engaged in risky injection and sexual behaviors, were less likely to have ever used a needle exchange, and were more likely to have recently experienced serious withdrawal symptoms. Those with a recent overdose were much more likely to have witnessed an overdose, to have known someone who died of an overdose, and to have experienced a prior overdose (92.2% vs. 33.7%).

In a multivariable logistic regression model (Table 2), characteristics and behaviors that were associated with an increased risk of experiencing an overdose in the past six months were using cocaine/crack in the past six months (OR, 2.07; 95% CI = 1.25 to 3.45), using alcohol in the past six months (OR, 1.90; 95% CI = 1.01 to 3.57), experiencing serious withdrawal symptoms in the past two months (OR, 2.70; 95% CI = 1.58 to 4.61), and having overdosed more than six months ago (OR, 28.58; 95% CI = 14.10 to 57.96). Younger age was associated with an increased risk of experiencing an overdose in the past six months. The c-statistic for the adjusted logistic

Table 1
Bivariate Associations between Demographic Characteristics, Health Status, Drug Use and Risk Behaviors, and Overdose Experience, and Overdose in the Past Six Months, among Heroin Injectors

	Total		Overdosed in Past Six Months		Did Not Overdose in Past Six Months	
	n	%	n	%	n	%
Total	772	100.0	128	16.6	644	82.4
Demographic characteristics						
Gender						
Male	600	77.7	107	83.6	493	76.6
Female	167	21.6	21	16.4	146	22.7
Age (yr)						
45+	132	17.1	15	11.7	117	18.2
35–44	296	38.3	43	33.6	253	39.3
25–34	288	37.3	55	43.0	233	36.2
18–24	56	7.3	15	11.7	41	6.4
Race/ethnicity						
White	88	11.4	16	12.5	72	11.2
African American	112	14.5	22	17.2	90	14.0
Hispanic	548	71.0	89	69.5	459	71.3
Asian or other race	24	3.1	1	8.0	23	3.6
Marital status	40.4	04.0	05	00.4	400	00 F
Never married	494	64.0	85 17	66.4	409	63.5
Married	115	14.9	17	13.3	98	15.2
Separated/widowed/divorced	162	21.0	26	20.3	136	21.1
Educational attainment Less than high school	389	50.4	64	E0.0	225	E0 E
High school/equivalent or higher	389	50.4 49.2	64 64	50.0 50.0	325 316	50.5 49.1
Homeless in past six months	300	49.2	04	50.0	310	49.1
No	237	30.7	26	20.3	211	32.8
Yes	454	58.8	90	70.3	364	56.5
Health status	434	30.0	30	70.5	304	30.3
Self-reported health						
Excellent/very good/good	301	39.0	39	30.5	262	40.7
Fair/poor	463	60.0	88	68.8	375	58.2
Human immunodeficiency virus status						
Negative	585	75.8	97	75.8	488	75.8
Positive	89	11.5	10	7.8	79	12.3
Unknown	97	12.6	21	16.4	76	11.8
SF-36 composite scores, mean (SD)*						
Physical functioning	74.4	(28.2)	72.3	(27.7)	74.8	(28.4)
Role limitations due to physical problems	56.8 (44.1)		44.8 (44.0)		59.2 (43.8)	
Role limitations due to emotional problems	52.8 (45.7)		41.7 (43.1)		55.0 (46.0)	
Social functioning	64.2	(31.7)	52.6	(31.6)	66.5	(31.3)
Bodily pain		(31.7)	51.7	(30.8)		(31.7)
Vitality	45.0 (23.3)		40.7 (22.6)		45.9 (23.4)	
General health	46.5 (16.5)		42.3 (17.2)		47.3 (16.2)	
Mental health	47.6	(22.6)	41.7	(21.1)	48.7	(22.7)
Drug use and risk behaviors						
Length of drug using career (yr)						
1–4	54	7.0	10	7.8	44	6.8
5–9	188	24.4	26	20.3	162	25.2
10–14	173	22.4	38	29.7	135	21.0
15–19	138	17.9	17 27	13.3	121	18.8
20+	219	28.4	37	28.9	182	28.3
Used cocaine or crack in past six months  No	386	50.0	42	32.8	344	53.4
Yes	386	50.0 50.0	42 86	32.8 67.2	300	46.6
Used alcohol in past six months	300	50.0	80	07.2	300	40.0
No	223	28.9	19	14.8	204	31.7
Yes	549	71.1	109	85.2	440	68.3
Used tranquilizers or benzodiazepines in past	343	7 1.1	103	03.2	740	00.3
six months						
No	566	73.3	78	60.9	488	75.8
Yes	206	26.7	50	39.1	156	24.2

Table 1
(continued)

	Total		Overdosed in Past Six Months		Did Not Overdose in Past Six Months	
	n	%	n	%	n	%
Number of types of drugs used in past						
six months						
1–5	272	35.2	26	20.3	246	38.2
6 or more	500	64.8	102	79.7	398	61.8
Any risky injection practices at last injection†						
No	440	57.0	58	45.3	382	59.3
Yes	327	42.4	70	54.7	257	39.9
Ever used a needle exchange						
No	254	32.9	53	41.4	201	31.2
Yes	458	59.3	68	53.1	390	60.6
Any sexual risk behaviors in past two months‡						
No	382	49.5	48	37.5	334	51.9
Yes	389	50.4	80	62.5	309	48.0
Heroin dependent§						
No	119	15.4	20	15.6	99	15.4
Yes	651	84.3	108	84.4	543	84.3
Cocaine dependent						
No	114	14.8	16	12.5	98	15.2
Yes	523	67.7	99	77.3	424	65.8
Serious withdrawal symptoms in past two months¶						
No	338	43.8	25	19.5	313	48.6
Yes	434	56.2	103	80.5	331	51.4
Methadone maintenance in past six months						
No	371	48.1	58	45.3	313	48.6
Yes	307	39.8	58	45.3	249	38.7
Detoxification in past six months						
No	292	37.8	48	37.5	244	37.9
Yes	471	61.0	78	60.9	393	61.0
Other drug treatment in past six months						
No	48	6.2	10	7.8	38	5.9
Yes	724	93.8	118	92.2	606	94.1
Overdose experience						
Overdosed prior to past six months						
No	437	56.6	10	7.8	427	66.3
Yes	335	43.4	118	92.2	217	33.7
Ever witnessed an overdose						
No	243	31.5	23	18.0	220	34.2
Yes	529	68.5	105	82.0	424	65.8
Ever personally known anyone who died						
of an overdose						
No	238	30.8	27	21.1	211	32.8
Yes	520	67.4	100	78.1	420	65.2

<sup>\*</sup> Short Form-36 (SF-36) component scores range from 0 to 100, with higher scores indicating better health.

regression model was 0.886, demonstrating the high predictive ability of this model.  $^{43}$ 

#### **DISCUSSION**

In this cross sectional study of current heroin injectors, we found that 16.6% had experienced at least one overdose in the past six months. Controlling for other risk factors, drug users reporting a prior overdose were 29 times more likely to have a recent overdose than those

not reporting a prior overdose. Other studies have demonstrated that most drug users who overdose experience multiple overdoses. 40,44 Much as a prior myocardial infarction strongly predicts a current myocardial infarction in the setting of anginal chest pain, these results suggest that clinicians' most important screening question for overdose prevention may be "Have you ever overdosed before?"

We found that current heroin injectors who reported using a variety of other drugs in the past six months

<sup>†</sup>Risky injection practices include splitting drug with needle and sharing cooker, cotton, rinse water, or needle.

<sup>‡</sup> Risky sexual behaviors include having a sexual partner with hepatitis, giving or receiving drugs or money for sex, using condoms less than 80% of the time with casual partners, and having more than one sexual partner.

 $<sup>\</sup>S$ Heroin dependence was indicated by a score of  $\ge$ 7 on the Severity of Dependence Scale.

 $<sup>\</sup>parallel$  Cocaine dependence was indicated by a score of  $\geq$ 3 on the Severity of Dependence Scale.

Serious withdrawal symptoms include stomach cramps, diarrhea, vomiting, and sweating.

Table 2
Unadjusted and Adjusted Models Predicting Overdose in the Past Six Months, among Heroin Injectors

	Una	Unadjusted		Adjusted*	
	OR	95% CI	OR	95% CI	
Demographic					
characteristics					
Age (yr)					
45+	1.00	_	1.00	_	
35–44		0.71, 2.48		1.34, 5.91	
25–34		1.00, 3.40		1.19, 5.05	
18–24	2.85	1.28, 6.35	7.20	2.54, 20.41	
Health status					
SF-36 composite scores†					
Role limitations due to	0.99	0.99, 1.00	1.00	0.99, 1.00	
physical problems					
Drug use and risk					
behaviors					
Used cocaine or crack in					
past six months					
No	1.00		1.00	_	
Yes	2.35	1.57, 3.50	2.07	1.25, 3.45	
Used alcohol in past six					
months					
No	1.00	_	1.00	_	
Yes	2.66	1.59, 4.45	1.90	1.01, 3.57	
No. of types of drugs					
used in past six					
months					
1–5	1.00	_	1.00	_	
6 or more	2.43	1.53, 3.84	1.67	0.93, 2.99	
Any sexual risk behaviors					
in past two months‡					
No	1.00		1.00		
Yes	1.80	1.22, 2.66	1.44	0.89, 2.32	
Serious withdrawal					
symptoms in past					
two months§					
No	1.00	_	1.00		
Yes	3.90	2.45, 6.19	2.70	1.58, 4.61	
Overdose experience					
Overdosed prior to past					
six months					
No	1.00		1.00	_	
Yes	23.22		28.58	14.10,	
		45.19		57.96	

<sup>\*</sup>Total of 768 participants had nonmissing values for all variables included in the adjusted model.

were more likely to have experienced a recent overdose, consistent with earlier findings that polydrug use is a strong predictor of both fatal and nonfatal overdose. <sup>4,15,18</sup> We also found that drug users who had recently experienced serious withdrawal symptoms were at greater risk for a recent overdose. These withdrawal symptoms may have resulted from voluntary or forced periods of abstinence, including incarceration or drug treatment

attempts, although we did not find an independent effect of enrollment in detoxification in the past six months on the risk of recent overdose, as demonstrated in other studies.  $^{23}$ 

In this sample, younger heroin injectors were at greatest risk of experiencing a recent overdose. Although this finding has been replicated in at least one other study, most studies have indicated greater risk of overdose among older users. A15,45 In these studies, age is often reflective of length of drug-using career, with overdose risk increasing as length of drug-using career increases; this analysis of recent overdose captured current rather than cumulative risk. It is also possible that in this sample, younger age reflected unmeasured exposures to social network characteristics that may increase risk of overdose, including larger networks and conflicts with network members or other unmeasured risk behaviors.

#### **LIMITATIONS**

These results must be considered preliminary due to several limitations. These data are not prospective, therefore the inferences that can be drawn regarding the predictive nature of characteristics and behaviors for overdose are limited. In addition, the timelines of some variables differ, with some referring to the most recent injection or behavior within the past two or six months. Although these most recent behaviors likely reflect consistent conditions and risk behaviors over the full duration of the relevant time period, because drug use and risk behaviors tend to be relatively consistent over time,47 this is not possible to demonstrate definitively. Intervieweradministered surveys are subject to social desirability bias, although other studies among drug users have demonstrated high validity in self-reported drug use and risk behaviors. 47-49 Recall bias may also be present in surveys, although this should be minimized by the focus on recent events. Some measures were used as proxies for the underlying measures of interest; for example, we did not have a direct measure of drug tolerance. Our measures of physical and mental health were limited to a general picture of perceived health and may not detect asymptomatic disease that may nonetheless contribute to risk of overdose. Finally, we assessed factors associated with recent nonfatal overdose; risk factors for fatal overdose may be different.

#### **CONCLUSIONS**

The strongest independent predictor of a nonfatal overdose among habitual heroin injectors was having had a prior overdose. Emergency physicians, often present during overdose management and revival, may have a unique opportunity to prevent future overdoses through, for example, referral to agonist maintenance treatment, delivery of overdose prevention education, or novel interventions such as prescription of take-home naloxone.<sup>30</sup> Prospective studies are needed to generate a rigorous model to predict future overdose risk among drug users.

 $<sup>\</sup>dagger$  Short Form-36 (SF-36) component scores range from 0 to 100, with higher scores indicating better health.

<sup>‡</sup>Risky sexual behaviors include having a sexual partner with hepatitis, giving or receiving drugs or money for sex, using condoms less than 80% of the time with casual partners, and having more than one sexual partner.

<sup>§</sup>Serious withdrawal symptoms include stomach cramps, diarrhea, vomiting, and sweating.

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# REFLECTIONS.

# They Go Back

Black eyes and guarded looks Really quite pretty The girl explained: I walked into a wall tripped up, fell down They are not convinced

Her man professes love with iron fists. Police are called Reports completed, papers filed As she protests

It makes no sense Exasperates them all One thing is understood: Before the ink is dry She'll go back

They always do

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