Wearable biosensors have the potential to monitor physiological changes associated with opioid overdose among people who use drugs: A proof-of-concept study in a real-world setting

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ABSTRACT

Introduction:

Wearable biosensors have the potential to monitor physiological change associated with opioid overdose among people who use drugs.

Methods:

We enrolled 16 individuals who reported ≥4 daily opioid use events within the previous 30 day. Each was assigned a wearable biosensor that measured respiratory rate (RR) and actigraphy every 15 seconds for 5 days and also completed a daily interview assessing drug use. We describe the volume of RR data collected, how it varied by participant characteristics and drug use over time using repeated measures one-way ANOVA, episodes of acute respiratory depression (≤5 breaths/minute), and self-reported overdose experiences.

Results:

We captured 1626.4 hours of RR data, an average of 21.7 daily hours/participant over follow-up. Individuals with longer injection careers and those engaging in polydrug use captured significantly fewer total hours of respiratory data over follow-up compared to those with shorter injections careers (94.7 vs. 119.9 hours, p = 0.04) and injecting fentanyl exclusively (98.7 vs. 119.5 hours, p = 0.008), respectively. There were 385 drug use events reported over follow-up. There were no episodes of acute respiratory depression which corresponded with participant reports of overdose experiences.

Discussion:

Our preliminary findings suggest that using a wearable biosensor to monitor physiological changes associated with opioid use was feasible. However, more sensitive biosensors that facilitate triangulation of multiple physiological data points and larger studies of longer duration are needed.

KEYWORDS

people who use drugs; wearable sensor; biosensor

1. INTRODUCTION

The opioid-related overdose epidemic is one of the most significant public health crises confronting the United States. Op oids accounted for 75% of the 90,000 overdose deaths from November 2019 – October 2020 (Ahmad et al., 2021; Center for Disease Control and Prevention, 2020) Interventions targeting this crisis have included overdose education and naloxone distribution programs (Walley et al., 2013), fentanyl test strips (Peiper et al. 2019), warm handoff programs that utilize peers to link recent overdose victims to drug treatment (Ashford et al., 2019), a smartphone-based application that link lay first responders to an overdose event (Schwartz et al., 2020), and remote supervised consumption spaces that connect people who use drugs (PWUD) to peer monitors by phone (Jean and Bonn, 2020; Perri et al., 2021). A common limitation among these interventions is that most required active engagement by the person who uses drugs (e.g., drug checking or requesting remote supervision) or from a nearby peer/responder (e.g., naloxone administration). Given more than half of

fatal overdoses occur when individuals use alone (Sherman et al., 2007; Siegler et al., 2014), novel interventions designed specifically for these events are needed.

Respiratory depression, slow heart rate, and physical inactivity are hallmark physiological changes associated with opioid overdose (Boyer, 2012; Chen and Ashburn, 2015). In clinical settings, wearable biosensors such as pulse oximeters or respiratory monitors are the gold standard for monitoring the physiologic impact of opioids. However, there is a dearth of information on whether wearable devices with remote sensing technology can reliably monitor these important op oid-related outcomes as individuals go about their daily lives. In this proof-of-concept study, we assessed whether a commercially available wearable biosensor could feasibly capture physiological changes associated with opioid overdose in a real-world setting.

2. METHODS

2.1. Setting and Partic pants

Data were collected from December 2019 – March 2020 in Philadelphia. Participants were recruited from UnityPhilly (Schwartz et al., 2020), a longitudinal trial of a smartphone-based opioid overdose intervention set in the neighborhood with the highest number of non-fatal and fatal overdoses and naloxone administrations in the city (Philadelphia Department of Public Health, 2020). Eligibility criteria for UnityPhilly were age ≥18 years, spending majority of your day in ZIP codes with high overdose rates, being able to read/write in English, owning a smartphone with an active data plan, and allowing the study team to access geolocation data (GPS coordinates). We used a two-

step process to recruit participants from UnityPhilly into the present study: research staff contacted UnityPhilly participants by phone or in-person who reported injection drug use within 30 days at their baseline (n=59); staff sequentially enrolled participants who met the following inclusion criteria: (1) snorting or injecting opioids at least four times daily for the past seven days, (2) willingness to wear a biosensor for 5 days, and (3) willingness to return to the study office each day of follow-up. Sixteen participants provided written informed consent and were enrolled in this pilot study.

2.2. Biosensor Provision and Collection of Physiological Outcomes

The research team reviewed 6 potential devices (Fuller et al., 2020) which included the Wavelet Health/Biostrap, Fitbit Cha ge 3, AutoSense, Oxitone, a smartphone sonar system (Nandakumar et al., 2019), and the Spire® Health Tag (Spire® Health, https://www.spirehealth.com/). We selected the Spire® Health Tag based on various factors: the one-year battery life, discrete size (5.6 cm x 1.3 cm x 0.5 cm), and unobtrusive placement (attached to underwear waistband for self-identified men or wing of bra for self-identified women). Participants were asked to wear the device consistently over the 5-day period, only removing it for the purpose of bathing. While the Spire® is active and touching the wearer's skin, it collects respiratory rate (RR) and physical movement, which is binned every 15 seconds with a 60 second sliding window, using a force sensor and 3-axis accelerometer, respectively, as well as heart rate every 4 minutes using a photoplethysmography sensor. After collection, the Spire® transmits data via Bluetooth to a secure cloud-based server and activity is recoded to active (>1 step within a 60 second bin) versus sedentary (0 steps within a 60

second bin). However, there were concerns that participants may not regularly have secure internet access and were asked to return to the study office daily for device placement verification as well as data download and transfer to a secure cloud-based storage.

2.3. Self-reported drug use and intoxication

Participants completed a daily timeline follow back (TLFB) nterview, a reliable method for capturing data on substance use in vulnerable populations (Hjorthøj et al., 2012). TLFB items had a 24-hour recall period and measured number of drug events, time of each event, drug(s) consumed at each event (e.g., fentanyl, heroin, powder cocaine, crack cocaine, methamphetamine, and benzodiazepines), route of administration for each drug consumed (e.g., injected, smoked, sniffed/snorted, and swallowed), dose (e.g., number of bags or pills), and resultant level of intoxication (e.g., too little, just right, and too much). For opioid-related “too much” events, we measured whether participants received any of the following interventions (yes/no): physical stimulation, naloxone, or had EMS called.

2.4. Measures and Statistical Analyses

2.4.1. Participant Characteristics

Over the study period, one participant was lost-to-follow-up (after third visit). Using R studio version 4.0.2 (R Core Team, 2020), we compared their pattern of drug use to those who completed the study. Their drug use pattern (i.e., primarily snorted heroin) differed from the remaining sample (i.e., primarily fentanyl injection); thus, we

decided to remove them from the present analyses. We then summarized key participant characteristics (i.e., age, gender, race/ethnicity, homelessness in past 30 days, years using injection drugs, lifetime overdoses, and perceived risk of overdose within the next year) drawn from the UnityPhilly baseline survey.

2.4.2. Biosensor Data

To assess feasibility, we downloaded data in a csv format ile (one file per participant) that contained information about the RR measured every 15 seconds. To assess feasibility, we summed the 15-second bins and calculated the total volume of RR data captured at the group-level over follow-up (1800 possible hours from 15 participants x 5 days x 24 hours), as well as daily average hours and 5-day total at the participant-level. We defined respiratory depression as ≤5 breaths/minute for 60 seconds as recorded by the Spire® (Nandakumar et al., 2019). Respiratory depression was computed over a sliding (moving) window 60 seconds, around the time of each reported drug use event (see Supplemental Materials for additional information on data management and visua ization of RR and physical movement). We used repeated measures one way ANOVA to assess for differences in the volume of RR data collected by participant characteristics and drug use pattern to explore emerging trends that may help design future studies.

2.4.3. Drug Use and Self-Reported Overdose

We calculated the total number of drug use events by route of administration and percentage of polydrug use (i.e., multiple drugs by various routes; yes/no) at the

participant-level over follow-up among the final sample (n=15). We summarized self-reported intoxication across drug use events and receipt of intervention (physical stimulation naloxone, or had EMS called) during events participants described as “too much”. For each “too much” event, we analyzed whether participants were active or sedentary or if RR fell below the predefined threshold for acute respiratory depression, based upon self-reported time of consumption from the TLFB.

2.5. Compensation and Ethics Approval

Participants received $10 for the initial enrollment and training visit, $20 for each completed follow-up visit, and another $20 for completing qualitative interviews during their 5th visit, a maximum total of $130 USD for the entire study. Study protocol was approved by the Drexel University Institutional Review Board.

3. RESULTS

3.1. Participant Characteristics

Most participants identified as non-Hispanic White (93%) and male (53%) with mean age of 42 (standard deviation [SD]=7.1; Table 1). The average length of drug injection career was 19 years (SD=7.5). The majority (87%) had experienced an opioid-related overdose in their lifetime and 27% believed they were somewhat or very likely to overdose again within the next year.

3.2. Biosensor Data

Out of 1800 possible hours, a total of 1626.4 hours of RR data were captured over follow-up which is equivalent to an average of 108.4 total hours (SD=15.6) or 21.7 daily hours (SD=3.1) per participant (Table 1). The volume of RR data collected was consistent over time, though participants with shorter injection careers had, on average, collected more total hours of data than those with longer injection careers (p = 0.04) as did individuals exclusively injecting fentanyl compared to those reporting polydrug use (p = 0.008). We did not detect any episodes of acute respiratory depression and thus, were unable to triangulate these data with movement.

3.3. Drug Use and Self-Reported Overdose

Via TFLB, we identified 385 drug administrations during the study period (Table 2), including 349 (91%) events in olving fentanyl. This translates to an average of 4.7 (SD=2.8) daily fentanyl injection per participant. Seven participants (46%) reported only fentanyl injection during the study period while the rest (54%) reported at least some sequential or simultaneous polydrug use (Table 1). There were 27/385 administrations (6.8%) after which participants characterized the intoxication level as “too much”. Among those, 23/27 were related to fentanyl injection. There were no self-reports of experiencing an opioid overdose, receiving naloxone, nor having EMS called. While among 5/23 events, participants reported needing physical stimulation to wake up, lack of escalation to the preceding measures suggest the level of sedation did not cause an overdose.

4. DISCUSSION

This proof-of-concept study is among the first to collect data on wearable biosensors that passively monitor physiological changes associated with opioid use in a real-world setting. Over the course of five days, the Spire® collected RR data for more than 90% of the total hours the device was assigned, suggesting that this may be a feasible manner of data collection among PWUD. This differs from prior work using the Spire® Stone (an older version of the device) among LinkedIn employees which indicated lower levels of engagement (Smith et al., 2019). Increased willingness to wear the Health Tag in our sample may be related to the device's less obstructive and discrete design (Kanter et al., 2021), sampling participants from UnityPhilly, and the high level of community awareness of ove dose risk in the Kensington neighborhood, which has been Philadelphia's epicenter for the opioid-related overdose crises. Furthermore, we found that individuals with longer injection careers and those engaging in polydrug use collected fewer hours of RR data. Moving forward, individuals in these groups may benefit from additional training on the device to improve data collection.

While our findings provide preliminary data on the feasibility of using the Spire®, there were limitations to the study design that could provide guidance for future research. Despite setting our study within real-world conditions, we were unable to validate our results with a gold-standard measure (e.g., video-recorded direct observation to evaluate physical activity) (Keadle et al., 2019). For instance, 10% of RR data was not captured by the device; however, we were unable to identify the source of missing data given that we did not directly observe when or how the device was worn.

User error (e.g., improper placement, removing the device to shower and forgetting to reapply) or device error (e.g., data not recorded) could be responsible for missing data. Future studies should consider periods where multiple devices are utilized to better characterize missingness.

Relatedly, we were limited in our ability to determine opioid-related overdoses. After reviewing changes in RR over time, we did not identify any events meeting our threshold for an acute respiratory depression nor were there any self reports of an opioid overdose (i.e., no reports of receiving naloxone). It is possible that this may be related to a pattern of lower-frequency, low-dose injection that is associated with a protective effect (Colledge et al., 2020) since our sample reported injecting an average of 1.4 bag of fentanyl per event (data not shown), despite an average of roughly 5 fentanyl injections per day. In qualitative exit interviews, participants indicated low volume use was a conscious act of harm reduction and reported using just enough to "get well" or mitigate withdrawal (unpublished results). For these reasons, along with the short duration of the study we did not capture any events meeting our definition of overdose and were unable to cross-reference RR with actigraphy data. Furthermore, we could not corroborate these results with heart rate given differences in the frequency in which it was captured over time. Future work might consider testing the wearable device to detect opioid-related overdoses in settings utilized by a large number of PWUD such as an overdose prevention facility.

5. CONCLUSION

Despite these limitations, this study provides important information about the potential role of wearable biosensors as a novel intervention to combat the overdose crisis. While most interventions require an active bystander, our data show that participants are willing to wear a device engaging in passive surveillance of physiological response to their opioid use which is promising. Critical next steps are to design and test a device more appropriate for detecting opioid-related overdose.

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Table 1. Volume of respiratory rate data collected by Spire® Health Tag, a commercially available wearable biosensor, by sociodemographic, drug use, and overdose characteristics (n=15)

	Number of RR Hours Captured by Biosensor Daily Mean (SD)							
	n	Day 1	Day 2	Day 3	Day 4	Day 5	5-Day Total (SD)[a]	F value[b]	P
Total sample	15	22.2 (5.7)	23.9 (0.1)	19.5 (9.1)	20.6 (8.4)	22.2 (6.2)	108.4 (15.6)		
Age, years								0.65	0.54
30 – 36	5	19.3 (9.8)	23.9 (0.1)	24.0 (0.1)	23.8 (0.5)	24.0 (0.1)	115.0 (9.0)		
37 – 45	5	23.9 (0.3)	23.9 (0.1)	15.7 (11.5)	19.2 (10.7)	23.6 (0.7)	106.2 (12.7)		

46 – 54	5	23.4 (1.2)	24.0 (0.1)	18.9 (10.6)	18.8 (10.5)	19.1 (10.7)	104.1 (22.6)		
Sex								1.56	0.23
Male	8	20.8 (7.7)	23.9 (0.1)	20.8 (8.3)	17.7 (10.9)	20.7 (8.4)	103.8 (18.6)		
Female	7	23.8 (0.5)	24.0 (0.1)	18.1 (10.3)	23.9 (0.4)	24.0 (0.1)	113.7 (10.1)		
Experiencing homelessness, 30 days								0.07	0.77
No	10	23.7 (0.8)	24.0 (0.1)	17.3 (10.6)	21.4 (7.5)	21.4 (7 5)	107.6 (17.6)		
Yes	5	19.2 (9.8)	23.9 (0.1)	24.0 (0.1)	18.9 (10 6)	23 9 (0.1)	110.0 (12.3)		
Length of injection career, years								4.18	0.04
9 – 14	5	23.9 (0.2)	24.0 (0.1)	24 0 (1)	24 0 (0.1)	24.0 (0)	119.9 (0.4)		
15 – 24	6	20.0 (8.9)	23.9 (0.1)	17 1 (10.9)	23.5 (0.8)	23.7 (0.6)	108.1 (11.7)		
25 – 31	4	23.3 (1.3)	23.9 (0 1)	17.5 (11.7)	12.0 (13.9)	17.9 (11.9)	94.7 (21.0)		
Number opioid overdose(s), lifetime								0.89	0.38
0	2	23.8 (0.3)	23.8 (0.2)	23.8 (0.1)	23.9 (0.2)	23.9 (0.2)	119.2 (0.1)		
1 – 2	6	20.1 (9.0)	24.0 (0.1)	20.0 (9.8)	23.5 (0.8)	23.9 (0.2)	111.4 (11.5)		
3 – 4	3	22.9 (1.4)	24.0 (0.1)	15.5 (13.3)	15.9 (13.8)	15.5 (13.4)	93.8 (26.1)		
5 – 50	4	24.0 (0)	24.0 (0.1)	19.6 (8.8)	18.0 (12.0)	23.9 (0.1)	109.5 (12.4)		
Perceived risk of overdose within next year								0.06	0.80
Very/somewhat unlikely	10	23.6 (0.9)	24.0 (0)	19.7 (8.8)	18.9 (10.0)	21.5 (7.6)	107.7 (17.3)		

Very/somewhat likely	5	19.3 (9.8)	23.8 (0.1)	19.2 (10.6)	23.9 (0.1)	23.6 (0.7)	109.8 (13.2)	
Total daily injections at follow-up								1.01 0.39
6 – 14	5	23.5 (1.2)	23.9 (0.1)	20.1 (7.7)	14.4 (13.1)	19.1 (10.7)	101.0 (21.3)	
15 – 24	5	19.6 (9.9)	23.9 (0.1)	24.0 (0)	23.6 (0.9)	23.9 (0.2)	115.0 (9.7)	
25 – 39	5	23.5 (0.6)	24.0 (0.1)	14.4 (13.1)	23.7 (0.4)	23.6 (0.7)	109 2 (13.3)	
Polydrug use over follow-up[c]								11.7 0.008
No	7	23.9 (0.2)	24.0 (0.1)	24.0 (0.1)	23.7 (0.8)	23.9 (0.2)	119.5 (0.9)	
Yes	8	20.6 (7.7)	23.9 (0.1)	15.6 (11.3)	17 8 (11.0)	20.7 (8.4)	98.7 (16.0)	

SD = standard deviation; TLFB = timeline foll w ba k.

[a] For each participant, we calculated the sum of daily number of hours captured by biosensor and subsequently estimated the mean of the s mmed hours for all participants

[b] Based on repeated measure one-way ANOVA

[c] Polydrug use (Yes = report ng f ntanyl, stimulants, benzodiazepines by various routes of administration over the course of a day vs. No = injection fentanyl only)

Table 2. Frequency of drug use and route of administration by participants, events, and average events reported per day collected from the timeline follow back interviews

	No. of Participants N (%)	No. of Events N (%)[a]	Average Daily Events (SD)[b]
Injected fentanyl only	15 (100)	277 (71.9)	3.7 (2.3)
Injected fentanyl and smoked crack cocaine, sequentially	5 (33.3)	55 (14.3)	2.2 (2.4)
Injected fentanyl and powder cocaine, simultaneously	2 (13.3)	30 (7.9)	3.0 (0.7)
Smoked crack cocaine only	2 (13.3)	17 (4.4)	2.1 (1.9)

Injected powder cocaine only	1 (6.7)	1 (0.3)	--
Injected methamphetamine only	1 (6.7)	4 (1.0)	1.3 (0.6)
Injected fentanyl and heroin	1 (6.7)	1 (0.3)	--
Smoked crack cocaine and used benzodiazepine, sequentially	1 (6.7)	1 (0.3)	--

[a] Calculated based on the total number of drug use events over follow-up, excluding methadone (N = 385)

[b] Number of events / (number of participants x 5 days of follow-up)

CONFLICT OF INTEREST

No conflict declared.

CRediT authorship contribution statement

AMR conceptualized the project and designed the study. NKT conducted the analysis. AMR and NKT wrote the initial manuscript All authors contributed to the interpretation of results, provided critical revisio s to the manuscript, and approved the final version to be submitted for publication.

HIGHLIGHTS

- A wearable biosensor was used to monitor respiratory rate among PWUD.
- Respiratory rate was captured for 1626.4 of 1800 possible follow-up hours.
- No instances of acute respiratory depression were detected.
- With refinement, biosensors could be used to intervene during solitary use events.