Autonomous Care Pathway to Patient Opioid Abstinence: Should All Programs Offer this Approach?

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ABSTRACT:

Introduction: The opioid epidemic resulted in vast increase in neonatal opioid withdrawal syndrome (NOWS). To mitigate NOWS and opioid dependency among women, staff established a gender specific, patient driven, autonomy based, outpatient therapeutic substitution program.

Methods: Prospective observational study of obstetric patients receiving prenatal care 7/1/2016-12/31/2019. Patients underwent universal urine drug screens to identify illicit drug use with dependency and offered addiction counseling with voluntary outpatient therapeutic substitution in an obstetrical-addictions combined clinic to achieve abstinence with oral Buprenorphine tapering protocol. Urine substance screening and cord blood testing were obtained at delivery. Birth outcomes compared among groups who achieved abstinence at birth, were successful at tapering, or continued opioid use.

Results: Of 783 births, 165 (20.9%) demonstrated opioid use with 91 (55.2%) participating at some point in pregnancy in therapeutic substitution program. At birth, 14/94 (14.9%) patients completed the program and achieved opioid abstinence, 22/94 (23.4%) still enrolled

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and actively tapering. 57/94 (34.5%) patients were lost to follow-up, relapsed, or terminated due to non-compliance. Seventy-four of 67 (44.3%) opioid positive mothers chose not to enroll. Of 14 women who completed the program, 0 babies born with NOWS, compared to 11/22 (50%) still enrolled in program and actively tapering, 29/57 (50.9%) lost to follow-up, relapsed, or terminated due to non-compliance, and 28/74 (37.8%) never enrolled in program.

***Conclusion/Implications*: Outpatient therapeutic substitution with oral Buprenorphine with abstinence is possible in pregnant patients and results zero NOWS. More data are needed to confirm findings and explore methods for enhanced success in obtaining abstinence.**

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The number of newborns treated for neonatal opioid withdrawal syndrome (NOWS), formerly known as the neonatal abstinence syndrome (NAS), has increased dramatically in West Virginia. In data collected from the Cabell Huntington Hospital in Huntington, WV, the number of neonates treated for NOWS increased from 25 in 2003 to 70 in 2007.[1] The mean cost difference in the care of an otherwise healthy neonate with NAS was compared to the cost of a normal full-term healthy neonate of $3,934 in the Cabell-Huntington cohort. Because of the added costs associated with the increased risk of prematurity and NOWS, the average cost of all infants with NOWS was over $36,000 compared to $2,000 for a NOWS-free neonate.[1] Therefore, pregnant patients present a unique opportunity to prevent NOWS and realize significant financial savings by decreasing the costs for neonatal care.

The previous data from CAMC presented by Hensel et al, 2012, found with universal urine screening for illicit substances in the CAMC obstetric and gynecologic residency clinic, that, 32% of pregnant patients were positive for illicit substances including 11% positive for multiple substances.[2]

The national substance abuse rates have been estimated to be between 2.8-19%.[3-5] These reported rates vary based upon the population screened and the method of screening used. In our own clinic experience, prior to universal urine drug screening using only a self-reported screening tool, zero of our patients reported any illicit substance usage. The lowest number reported is in the study by Ebrahim and Gfroerer utilizing a population survey of the entire United States[3] while the highest rates were reported (19%) by Azadi and Dildy utilizing urine toxicology testing.[5] Chasnoff et al developed a self-reporting screening tool that estimated that 15% of the population studied continued to use substances of abuse after becoming aware of the pregnancy.[4]

Neonatal opioid withdrawal syndrome may be present in 60-90% of neonates exposed in-utero to opioids with up to 70% of affected neonates exhibiting central nervous system irritability which may progress to seizures.[6] Up to 50% of exposed neonates may experience respiratory issues, feeding problems, severe diarrhea, inconsolability, and failure to thrive.[7] A randomized controlled study of 175 pregnant patients (89 Methadone/86 Buprenorphine) comparing Methadone to Buprenorphine by Jones et al, 2010 found that 41/75 (57%) of neonates had NOWS with Methadone and 27/58 (47%) of neonates had NOWS with Buprenorphine.[8] The Buprenorphine cohort had shorter hospital stays (10.0 days versus 17.5 days $P<0.0091$) and shorter days of treatment for NOWS (4.1 days versus 9.9 days, $P<0.003125$)[8] Treatment of NOWS represents a substantial hospital cost and significant effect on newborns with accepted treatment modalities.

Due to the morbidity to neonates and families with NOWS, we developed a voluntary program to prevent NOWS. Further, our patients expressed a desire to prevent NOWS in their neonates and to become opiate abstinent. Outpatient weaning from opiates had previously been considered impossible. The American College of Obstetricians and Gynecologists (ACOG) and Substance Abuse and Mental Health Services Administration (SAMHSA) both support medication assisted treatment (MAT) as the standard of care and discourage abstinence due to concerns about relapse.[9,10] Their positions rest on papers such as Terplin et al 2018 which reported that MAT should be the standard of care base on their review of the literature. However, Terplin's review consisted of patients primarily in inpatient settings, those who did not undergo fetal monitoring, patients with poorly defined counseling/adherence in the papers reviewed, and studies involving involuntary patient participation.[11] ACOG and SAMHSA simply did not engage the concerns regarding cognitive and behavioral impact, including NOWS, on neonates exposed to opioids.

Methods and Materials

Patient Autonomy

The American College of Obstetricians and Gynecologists strongly supports patient autonomy and informed consent as consistent with ethical care of patients.[12] The acceptance by ACOG of Jonsen's four principles-"four box" model of ethics (autonomy, beneficence, non-maleficence, and justice) displaces more traditional normative ethical theories.

The traditional historical ethical theories are generally divided into the Consequentialist Framework; The Duty Framework; and the Virtue Framework. The Consequentialist Framework focuses on the future effects of the possible courses of action, considering the people who will be directly or indirectly affected. It is then asked about what outcomes are desirable in a given situation, and consider ethical conduct to be whatever will achieve the best consequences (i.e. lying to protect Jews from Nazis). The Duty Framework focuses on the duties and obligations that exist in a given situation, and consider what ethical obligations are inherent and what things should

never be done (i.e. murdering someone). Ethical conduct is defined by doing one's duties and doing the right thing, and the goal is performing the correct action. The Virtue Framework focuses on person rather than action based: it looks at the virtue or moral character of the person carrying out an action, rather than at ethical duties and rules, or the consequences of particular actions (i.e. the practice of honesty on all dealings). A good person is someone who lives virtuously—who possesses and lives the virtues. The ignoring by ACOG of alternative ethical theories presupposes that they speak as the only authoritative voice when dealing with complex clinical issues such as substance abuse disorder (SUD) in pregnancy.

We utilized both Jonsen's four box model of autonomy/beneficence and Duty Framework Ethics to develop our treatment program. In support of respecting patient autonomy with regard to treatment options, we developed a voluntary outpatient Office-Based Medication Assisted Treatment Program (OBMAT) to secure patient abstinence. The instigation of such an OBMAT program aligns with ACOG Committee Opinion #390 regarding patient autonomy as an important cornerstone of ethical care of our patients.[12] Without any "choice" for a patient, there can be no autonomy since autonomy presupposes a choice between options. If there is no option present except MAT without abstinence, there is no exercise of autonomy. This would violate ACOG's ethical positon in Committee Opinion #390 regarding patient autonomy. Therefore, our program sought to prevent NOWS by honoring patient autonomy. We sought to use a gender specific, voluntary patient-centered, autonomous therapeutic substitution OBMAT program to achieve patient abstinence, thereby avoiding the neonatal hospitalizations, and costs associated with the use of Methadone and Buprenorphine maintenance therapy without abstinence. With regard to beneficence, we sought to contribute to both the welfare of the patient and her fetus by preventing NOWS and rendering the patient abstinent. The Duty Framework allowed our program to focus on our goal of performing the right action: preventing NOWS and achieving patient abstinence while honoring patient autonomy.

The purpose of our study was to evaluate the impact of gender specific care with patient respecting autonomy on the voluntary enrollment in a program designed to utilize therapeutic substitution to achieve maternal abstinence and thereby avoid NOWS.

Enrollment

All obstetric patients screened in our clinic were offered an opportunity to enroll in our abstinence-based program. Those who declined continued in their present programs, or were referred to other maintenance programs.

All patients received the same obstetrical care regardless of their choice of substance program. Patients who elected to enroll in our voluntary therapeutic substitution program from 1 July 2016-31 December 2019 in the CAMC resident obstetrics clinic, participated in an intensive multidisciplinary approach to prenatal care. Our plan of care included: weekly and random urine drug screening, a double board certified-addictions medicine/maternal-fetal medicine physician, a certified substance abuse counselor, ob-

stetrical staff/resident physicians, trained nursing personnel, and a nursing educator. Key in the management of all of our obstetrical patients' care was routine screening of patients' initial urine for illicit and non-prescribed substances. All patients who tested positive for non-prescribed (including tobacco and marijuana), or illicit substances, were counseled for voluntary enrollment in our abstinence-based addictions program including our contingency management program for substance abuse staffed by a certified addictions specialist. Weekly combined obstetric and addiction visits to the high-risk obstetrical clinic were included throughout the pregnancy and thereafter as dictated by the patient's obstetric and recovery needs. Patients had weekly group therapy alongside other women with substance use disorder, as well as monthly individual therapy addressing the entirety of the patient's psychosocial well-being. Obstetric management for all patients, whether in our program or not, included thorough fetal anatomic surveys, as well as fetal echocardiograms, antenatal testing, serial growth ultrasounds, and fetal umbilical artery Doppler studies, all as clinically indicated. Delivery was generally performed at 39 weeks gestation, or, as clinically indicated for obstetrical reasons.

Testing of patients' urine weekly during the program and with random drug screens for illicit substances continued throughout their obstetrical care. Patients who took opiates, and were at risk for acute opiate withdrawal, received therapeutic substitution with Buprenorphine medication to obtain abstinence. Careful attention to the use of other illicit medications paralleled the substitution of Buprenorphine for illicit opioids. Significant interactions with other medications, including patient mortality, occur with buprenorphine with concurrent abuse/use of benzodiazepines, other opioids, SSRIs, Benadryl, cocaine, and methamphetamine. Patients with persistent use of these medications and/or elicit medications would be removed from the program. Patients failing to adhere to the OBMAT program guidelines were referred to other programs for addiction care but received ongoing obstetrical care in our clinic. Further, patients who tested positive for illicit substances, who provided care for minor children, and, were deemed to be a danger to their children, underwent state directed mandatory reporting to child protective services to prevent child endangerment.

The program utilized outpatient therapeutic substitution with decreasing dosages of Buprenorphine with weekly group meetings which focused on improving coping skills and increasing distress tolerance. (See Table 1). Patients' urines were screened weekly and confirmed with mass spectrometry testing to ensure compliance with care. Detailed tapering schedules were individualized based on patients' gestational age and opiate requirements. None of our patients underwent any form of acute "detoxification" from their opioid medications. Rather, patients' dosages were slowly adjusted by decreasing by 2 mg of Buprenorphine over several weeks (usually 3 weeks at a given dose) until they were abstinent at least 1 week prior to delivery. (See Attachment 1). We chose at least one week prior to the anticipated delivery date due to the long half-life of Buprenorphine of approximately 96 hours.

The therapy component of the program consists of both psycho-educational and cognitive-behavioral therapy. Patients were educated on the disease concept of

Table 1: Prenatal Positive Substance Screens (n=783)

	n (%)
Substance Screen Positive*	557 (71.1)
Cotinine	415 (53.0)
Marijuana	326 (41.6)
Buprenorphine	131 (16.7)
Norbuprenorphine	113 (14.4)
Amphetamine	95 (12.1)
Methamphetamine	95 (12.1)
Oxycodone	16 (2.0)
Oxymorphone	19 (2.4)
Methadone	8 (1.0)
Morphine	38 (4.8)
Cocaine	16 (2.0)
Benzodiazepines	66 (8.4)
Ecstasy	0
Barbiturates	0
Phencyclidine	0
Multiple Substances *	351 (44.8)

*These calculations do not include tobacco use

addiction, the recovery process, relapse prevention, and the effects of drugs on the baby. A contingency management program, an evidence based practice with roots in Motivational Interviewing, was utilized to keep patients engaged in their abstinence process. Contingency management therapies are a type of psychosocial intervention where clients receive rewards in the form of vouchers or prizes if they demonstrate changed behaviors. Data supports contingency management therapy in cocaine and opioid abuse.[13-16] It has also been shown to be effective in the vulnerable populations of co-occurring psychological disorders and in pregnant women.

Analysis of the delivery outcomes in patients screening positive for substance abuse in pregnancy was performed. The study was approved by the joint Charleston Area Medical Center-West Virginia University IRB.

Results

During the study time period, there were 783 births at our tertiary care medical center from mothers receiving prenatal care in our affiliated resident service clinic. The majority of these neonates (557; 71.2%) were exposed in utero to substances including, illicit drugs, alcohol, marijuana, and tobacco, and were assessed via universal substance screening throughout prenatal visits. Table 1 summarizes the percent of specific substance exposures, with very high rates of cotinine (tobacco) 52.6% and marijuana 41.4%.

Study groups were divided into four arms. The first group included those who successfully completed the program and were opioid abstinent at the time of childbirth (1). The second group included those who were enrolled in the program and compliant but were still tapering (2). The third group included patients who chose to voluntarily withdraw from the program, were terminated due to continued noncompliance (use of known dangerous substances listed above with buprenorphine), transferred to another program, or who completed tapering successfully and then continued to use opiates illicitly (3). The fourth group consisted of those patients who did not elect to participate in therapeutic substitution. (4). Women who did not test positive for opiates in prenatal care were not included in the study groups.

The number of neonates exposed to opioids during prenatal visits was 167/783 (21.3%), of these mothers of 94/167 (56.3%) neonates voluntarily participated in the therapeutic substitution program at some point in gestation. At time of birth, 14/94 (14.9%) neonates had mothers who completed the program and achieved opioid abstinence at the time of birth, 22/94 (23.4%) were still enrolled and actively tapering. Mothers of 57/94 (34.5%) neonates were either lost to follow-up, relapse, or termination due to non-compliance. Finally, of the 167 opioid positive mothers, 74/167 (44.3%) chose not to enroll in the program.

Of the 783 births, a total of 71 (9.1%) babies were born with NOWS. The majority of mothers were White, with a rate of over 10% having babies with NOWS, compared with 3.1% for Blacks/African Americans, $p=0.027$. Most mothers with NOWS affected neonates were multiparous and this rate was statistically significant at 76.1%, $p<0.001$. Associated tobacco use was statistically more likely in mothers with NOWS affected neonates at a high rate of 80.3%, as compared with 49.7% tobacco use in mothers of NOWS free babies, $p<0.001$. Conversely, marijuana use rates were higher among mothers with babies without NOWS, 42.3% versus 28.2% for those with NOWS, $p=0.014$. Other maternal characteristic comparisons are detailed in Table 2.

Of the 14 women who successfully completed the program, 0 babies were born with NOWS demonstrating the ability to successfully to achieve outpatient abstinence at patient's request and prevent NOWS. These findings of zero neonates born with NOWS validated the autonomous decisions of the patients to voluntarily enter the OBMAT program to achieve abstinence. Of those who did not achieve abstinence, 11/22 (50%) were still enrolled in the program and actively working toward tapering, 29/57 (50.9%) were either lost to follow-up, relapsed, or terminated due to non-compliance, and 28/74 (37.8%) were never enrolled in the program (see Figure 1). There is a statistically significant difference when comparing program status with rates of NOWS ($p=0.004$).

The goal of the program was to achieve opioid abstinence at birth per patients' request to avoid NOWS and validate patient autonomy. To measure the success of the program, a comparison was made between all four groups and the rate of negative illicit opiate drug screens at birth (see Figure 2). This excluded Buprenorphine prescribed as part of a Medication-Assisted Treatment program. This was a statistically significant comparison with regard to opioid positive testing in labor [$p<0.001$], with 1/14 (7.1%)

Table 2: Maternal Characteristics of Newborns and NOWS Status (n=783)

	No NOWS (n=712)	NOWS (n=71)	p value
	n (%)	n (%)	
Race/Ethnicity			0.027
White	581 (89.7)	67 (10.3)	
African American	124 (96.9)	4 (3.1)	
Asian American	5 (100.0)	0 (0.0%)	
Latino American	1 (100.0)	0 (0.0%	
Parity			<0.001
Nulliparous	206 (28.9)	17 (23.9)	
Multiparous	506 (71.1)	54 (76.1)	
Diabetes	58 (8.1)	1 (1.4)	1.00
Psychiatric Disorders	158 (22.2)	18 (25.4)	0.552
Cotinine	354 (49.7)	57 (80.3)	<0.001
Marijuana Use	301 (42.3)	20 (28.2)	0.023

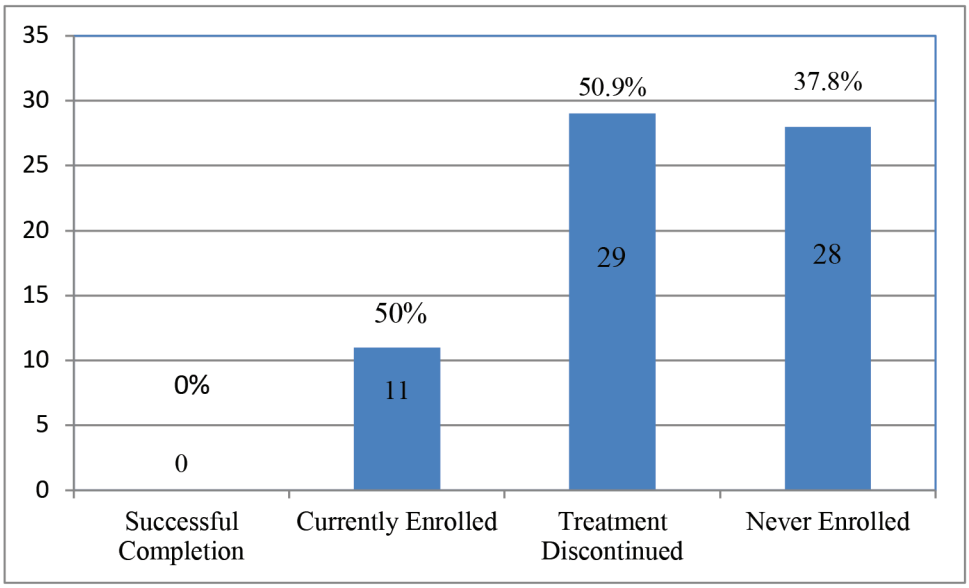

Figure 1: Neonates Free of NOWS by Program Status at Time of Delivery (p=0.004)

of mothers testing positive who completed the program, 2/22, (9%) testing positive of tapering mothers, 33/57, (57.9%) testing positive of terminated/transfer/lost to follow

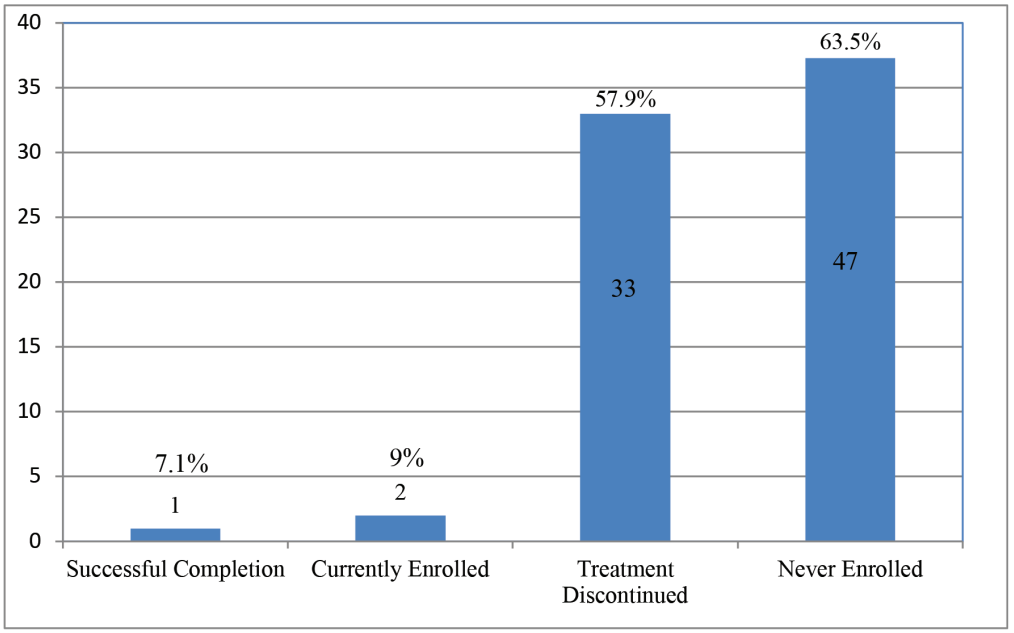

Figure 2: Positive Illicit Opioid Drug Screens at Birth by Program Status ($p<0.001$)

up, and 47/74, 63.5% of non-program mothers testing positive for illicit opiates at the time of delivery. Of note, the one mother who tested positive for illicit opiate use from the successful opioid treatment completion group (1/14), received morphine in labor for pain control, and therefore, tested positive due to opioid medication used for pain therapy during labor.

There were 3 neonates with NOWS born to women who tested negative at prenatal care and were therefore not eligible for enrollment in our OBMAT program. Women with negative opioid drug testing both during prenatal care and at birth had 0 births with NOWS. Conversely, women using substances throughout gestation with positive opioid drug tests both during prenatal care and at birth had the highest number 51/218 (23.4%) of babies with NOWS. Women who tested negative prenatally and then positive at birth had a 13.3% (4/30) NOWS rate. This is in comparison to women who tested positive prenatally and negative at time of birth with a 4.7% (16/344) NOWS rate, thus demonstrating the importance of abstinence at time of delivery. (See Table 3) No adverse outcomes were noted in any patients or neonates who entered and/or completed our program. If you take a rate of NOWS at 50% with opiate use then there would have been 7 neonates in the completed abstinence program group that should have had NOWS without therapeutic substitution. With the actual number at 0, this program prevented 7 additional babies with NOWS. Cost savings for the 7 neonates born abstinent is estimated at over $200,000 in hospital costs alone.[1] Detailed cost analysis for our program was not available but is an area to consider for further investigation.

Table 3: NOWS by Prenatal and Birth Test Results (Neg or Pos)

	Neg UDS at Initial Appointment & Neg UDS at Birth (n=197)	Pos UDS at Initial Appointment & Pos UDS at Birth (n=218)	Pos UDS at Initial Appointment & Neg UDS at Birth (n=344)	Neg UDS at Initial Appointment & Pos UDS at Birth (n=30)
	n (%)	n (%)	n (%)	n (%)
Instances of NOWS	0 (0.0)	51 (23.4)	16 (4.7)	4 (13.3)

There were no statistically significant differences in Neonatal Intensive Care Unit (NICU) admission, Pre-term birth (PTB) defined as birth before 37 weeks gestation, Intrauterine Growth Restriction (IUGR), Low Birth Weight (LBW) defined as <2500 gm, Pre-eclampsia, and Respiratory Distress Syndrome (RDS).

Discussion

In our obstetric population, we found a surprising 557; 71.2% of our patients with illicit or non-prescribed substances (including tobacco) in their urine at initial prenatal visit with utilization of universal screening. This is in contrast to the use of illicit or non-prescribed substances reported in previous studies in the general population of 3-19 %.[3-5] It is believed that our increased rates of substance use are partly explained by universal screening (including for marijuana) compared with the use of questionnaires in many studies. Using our novel approach of patient-requested, autonomous oral therapeutic substitution with Buprenorphine and contingency management in conjunction with a certified addictions counseling, we had 14 births to mothers who successfully completed the program and 0 of the neonates had NOWS. This low rate of abstinence (15%) among our program patients reflects the challenges faced with substance abuse disorder and other chronic illnesses. For example, only 20% of individuals who engaged in weight loss maintain their weight over time.[17] Chronic hypertension presents another example. A study by Vrijens et al 2008 using database information from Belgium found that 50% of patients stopped their antihypertensive by one year and that of patients who were taking medications, at least 10% were omitting single or multiple doses.[18] Diabetes care compliance appears similar to substance abuse with Koro et al 2013 finding only 11-18% of patients in their study maintaining their diabetes medication usage.[19]

Our success mirrors the previous experience of Luty, et al 2003 which studied 101 opiate dependent women who underwent a 21-day Methadone inpatient withdrawal with no adverse effects found.[20] However, only ten of the patients in Luty's sample were completely weaned off Methadone and only 1 was drug free at delivery.

Our data also replicates Stewart et al, 2013 who utilized a slow Methadone inpatient taper for pregnant inpatients without any associated morbidity or mortality.[13] Their group found that 53/96 (56%) of patients could successfully be detoxified as inpatients.

Finally, Bell et al, 2016 published on 301 pregnant patients who were fully detoxified using Buprenorphine in both inpatient and outpatient settings with no adverse maternal or neonatal outcomes.[21]

Our data is in contrast to a recent systematic review by Terplan et al 2018, which purported that "detoxification" as a treatment recommendation in pregnancy was not supported by their review.[11] Their review consisted of patients primarily in inpatient settings, who did not undergo fetal monitoring, poorly defined counseling/adherence in the papers reviewed, and some studies involved involuntary patient participation.[11] In contrast, our patients voluntarily participate in gender-specific, outpatient, autonomous therapeutic substitution with adjustment of medication to achieve abstinence, undergo weekly group addictions counseling sessions, at least monthly individual counseling, and participate in weekly and random urine drug screening. They also participate in weekly high-risk obstetrical prenatal visits and receive comprehensive prenatal diagnostic ultrasounds for anatomy/fetal echocardiograms, undergo serial growth ultrasounds, antepartum assessment by non-stress testing/AFIs/BPPs, and umbilical artery Doppler studies, all as indicated. Our patients are screened at delivery for substances, and neonates are screened at delivery. Further, all neonates were evaluated for NOWS by our neonatologists using the Finnegan scoring system.[22]

Radiologic and Behavioral Findings

MRI studies of postmortem and quantitative brain studies found smaller brains and decreased volumes including the cerebral cortex, amygdala, accumbens area, putamen, pallidum, brainstem, and cerebellum in neonates born to mothers exposed to heroin.[23] Sirnes et al 2017 compare volumes in 16 opioid exposed children ages 10-14 years to controls and found smaller brain volumes in the basal ganglia, thalamus, and cerebellar white matter.[24] Yuan et al echoed these findings documenting smaller whole brain and basal ganglia volumes compared to controls.[25] Monnelly et al 2017 compared 20 methadone exposed neonates to 20 non-exposed neonates via diffusion tensor imaging and found differences in white matter microstructure in the superior longitudinal fasiculus responsible for connecting the frontal, occipital, temporal and parietal lobes of the brain.[26] Altogether, this data validates serious concerns regarding fetal opioid exposure in utero (including buprenorphine) with regard to brain growth in utero and subsequent neurodevelopment after exposure. These concerns for adverse neurological outcomes appear inadequately addressed in the ACOG and SAMSHA position statements and care guidelines for MAT in pregnancy.

One study regarding mental development of 72 neonates (without other prenatal risk factors) found IQ differences at 1, 2, 3, 4.5 and 8.5 years of age.[27] Boys had lower IQ scores than girls. Cognitive functioning remained lower in all children exposed to opioids compared to controls even after accounting for socioeconomic status, adoption, foster care placement, gestational age at delivery, and birth weight.[27] Children diagnosed with NOWS after delivery exhibited twice the likelihood of conduct disorders; including attention-deficit/hyperactivity, adjustment, and intellectual disabilities.[28] These children

were also 1.5 times more likely to be diagnosed with developmental delays, anxiety, emotional disturbances, and autistic disorders compared to controls.[28] Buprenorphine, however, appears to be associated with a decreased risk of low birth weight and smaller head circumference, but, with more preterm births compared to methadone.[29] The effects of buprenorphine on both fetal brain development and behavior are not well studied.

ACOG and SAMSHA also appear to ignore the literature documenting increased risk of congenital heart defects, hydrocephalus, and neural tube defects in prenatal opioid exposure.[30]

Concerns for achieving abstinence appear unwarranted. A study by Luty, et al 2003 with 101 opiate dependent women tapered 21 pregnant patients off opiates without ill effects.[20] More recently Bell et al, 2016 reported more than 600 patients detoxified from opiates during pregnancy with no report of fetal harm related to the process.[21] We sought to build upon this literature with the development of our voluntary gender specific autonomy based program.

Most striking in our study was the financial analysis, which revealed over $200,000 estimated savings for the NICU hospital stays in our hospital associated with the 14 drug-free neonates based on the previous NICU cost data for neonates who did not require any withdrawal therapy or care for neonatal abstinence.[31] This does not include the substantial cost savings and decrease in morbidity associated with a neonate born drug free.

Comorbidities with multiple psychiatric disorders in patients with substance use disorder must also be considered. Many patients with substance use disorder have affective disorders including: depression, mania, schizoaffective disorders, schizophrenia, borderline personality, and bipolar disorders. Therefore, many authors suggest that detoxification must be linked with a combination of behavioral therapy with contingency management therapy with certified addictions counseling as in our patients.[23-26] Our behavioral therapy relies on counseling with certified addictions counselors, to assist patients in remaining drug and alcohol free.

Due to the large number of patients affected in the state of West Virginia and in our population at CAMC by substance abuse, we followed a patient centered, autonomous, programmatic, multidisciplinary approach with the use of outpatient abstinence therapy and therapeutic substitution with Buprenorphine when necessary. Inpatient therapy and stabilization was used when indicated in select patients. Therefore, in distinction to ACOG's recommendations,[9] and the findings of Terplan et al,[11] we demonstrate that gender-specific, patient centered outpatient treatment for opioid addiction should be considered in spite of the low completion rates and uncertain relapse rates. Further, since patient autonomy remains a cornerstone of women's healthcare today, patients ought to at least be offered an opportunity to deliver their infant completely drug-free and abstinent without NOWS.

Limitations to our study include low total enrollment rate of 56.3% (94), a relatively high dropout rate 34.5%, and a significant number of patients (16) transferring to other opioid maintenance programs for which we did not have any information on program compliance. We have not been able to demonstrate longer-term follow up post-partum, which is a limitation in assessing the long-term effectiveness of the program. Strengths include that despite low enrollment, over 10% (14.9%) of patients achieved complete abstinence, and hence, a decreased NOWS rate. Additionally, patients who did not comply with weekly drug testing were dismissed from the program with referral to outside programs, allowing the capture of more accurate drug usage data. Despite losing patients to failed compliance or transfer to other programs, many of the patients delivered at our hospital, thus allowing us to capture their birth outcomes and drug testing upon delivery. We also do not have detailed information regarding patient decisions process for enrollment other than to achieve abstinence. The participation in our program could be a surrogate for difficulty with other programs, desire to avoid child protective services, obviate possible legal actions/incarceration, and desires to please providers.

Patient requested-autonomous gender-specific outpatient therapeutic opioid substitution to obtain abstinence appears to be a reasonable and achievable approach alongside treatment of the psychological co-morbidities associated with substance use disorder. Multidisciplinary clinics with a single location for services would appear the ideal solution with the combination of excellent onsite medical care, antepartum fetal diagnostic services, antepartum fetal assessment, board certified addictions physicians/counselors, psychiatric support, and social support necessary to deliver drug-free mothers with healthy drug-free neonates. Increased compliance with outpatient programs may be enhanced by patients and families participating in long-term residential recovery programs, designed for restoration from addiction while undergoing therapeutic substitution.

Gender-specific treatment and public health-oriented approaches emphasizing, that, in spite of the chronic nature of addiction, women should be offered an opportunity at abstinence to prevent NOWS. In spite of the uncertain relapse rates associated with abstinence attempts, the dialogue involving opioid use disorder in women ought to be modified to elucidate that effective treatment for abstinence should be offered to prevent NOWS along with efforts to enhance comprehensive women-centered treatment availability and accessibility to improve maternal and neonatal outcomes within the perinatal period.

Finally, obvious significant financial savings (over $200,000 in NICU costs alone) may be realized from this programmatic approach to abstinence therapy, as well as providing an autonomy affirming choice to our pregnant patients. Such large savings may be actualized to enhance services with case management and increased support services for pregnant women with substance use disorder.

Further study is needed to evaluate if such outpatient programs help prevent relapse in patients postpartum.

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Attachment 1 Suggested Guidelines for Opioid Therapeutic Substitution*

1) Background
   a) 10-14% of women use illicit drugs in pregnancy.
   b) Neonatal abstinence syndrome (NAS) increases average cost of delivery from $2,000 to over $36,000 (18 times).
   c) 2009 Anonymous cord study at 8 hospitals found 115/759 (15%) positive for substances.[1]
2) Treatment
   a) Previous literature from 1970's and up to early 1990's suggested avoidance of detoxification.
   b) Recent literature does not substantiate these claims.
   c) Study by Luty, et al 2003 with 101 opiate dependent women, of which 21 underwent acute withdrawal without ill effects on pregnancy.[2]
   d) Our program also does not acutely withdraw patients, but rather offers slow therapeutic substitution which is not associated with acute withdrawal symptoms.
3) CAMC Women's & Children's Outline for Therapy
   a) Universal urine drug screening (UDS) with confirmatory testing for all new obstetrical patients.
   b) All patients testing positive for illicit substances are seen in high risk clinic. THC has a quantitative analysis.
   c) All patients with positive tests are offered a visit with our addictions counselor for evaluation for therapeutic substitution program and need for group therapy. If THC positive patient has a level < 150 ng/mL, they are placed in a routine clinic and re-screened with urine screens periodically.
   d) All other positive testing results are offered referral to our addictions counselor for for group sessions/therapy with our addictions counselor. Therapy sessions follow a DBT model and 12 step philosophy and incentives are given to patients to encourage and reward participation.
4) Therapeutic Substitution
   a) If patients are opiate dependent, found by our addictions counselor to be eligible for outpatient opiate therapy and request therapeutic substitution, they are offered therapeutic substitution with decreasing Buprenorphine (Subutex) dosing until abstinent.
   b) Patients on Methadone must be decreased to 30 mg or lower of Methadone and be off Methadone for approximately 36- 48 hours prior to attempting opiate therapeutic substitution due to significant adverse drug interactions.
   c) Patients on short-acting opiates may be started immediately on Buprenorphine (Subutex).

d) Patients on heroin generally need to be abstinent from heroin for approximately 12-24 hours prior to initiation of treatment due to interactions with Buprenorphine (Subutex).
e) The therapeutic protocol treatment dosage is gauged by amount of opiate the patients have been self-reporting for their use.
f) Patients generally start between 8-16 mg of Buprenorphine daily. We generally start at 8 mg as the induction dose and asses the patient's symptomatology.
g) After induction and stabilization, Buprenorphine (Subutex) dose is then decreased in 2 mg increments until patients are abstinent from Buprenorphine (Subutex).
h) Dose reduction is initiated no more than weekly, with timing individualized to the patient's motivation and time remaining until expected delivery.
i) We attempt to have patients weaned off Buprenorphine approximately 1 week prior to their estimated delivery date due to the long half-life of Buprenorphine of approximately 96 hours.
j) Patients are screened every week with stat UDS and random UDS done at the discretion of providers. Positive screens for illicit substances are sent for confirmatory testing with mass spectrometry. Positive testing triggers an intervention with the patient and potential for termination from program with referral to a maintenance based Buprenorphine program.
k) Every patient must attend weekly group addiction therapy sessions and at least one individual therapy session a month. Medications are dispensed only after attending group sessions.

5) Special Considerations
   a) Higher doses of opiates may necessitate starting at 16 mg of Buprenorphine (Subutex) per day.
   b) Patients must not be taking ***ANY*** other opiates, benzodiazepines, or other illicit drugs at induction of the Buprenorphine due to the severe interactions.

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