

Demystifying Suboxone

A Brief Primer for Primary Care Providers

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Disclosures

- I'm a physician in private practice
- I was previously employed by
 - HealthEast Care System (medical director)
 - North Memorial Health Care (vice president)
- I'm on faculty at the University of Minnesota
 - Evidence-based medicine
- I don't have any financial relationships with the pharmaceutical or medical device industries
- I don't intend to discuss investigational drugs or the “off label” use of medications

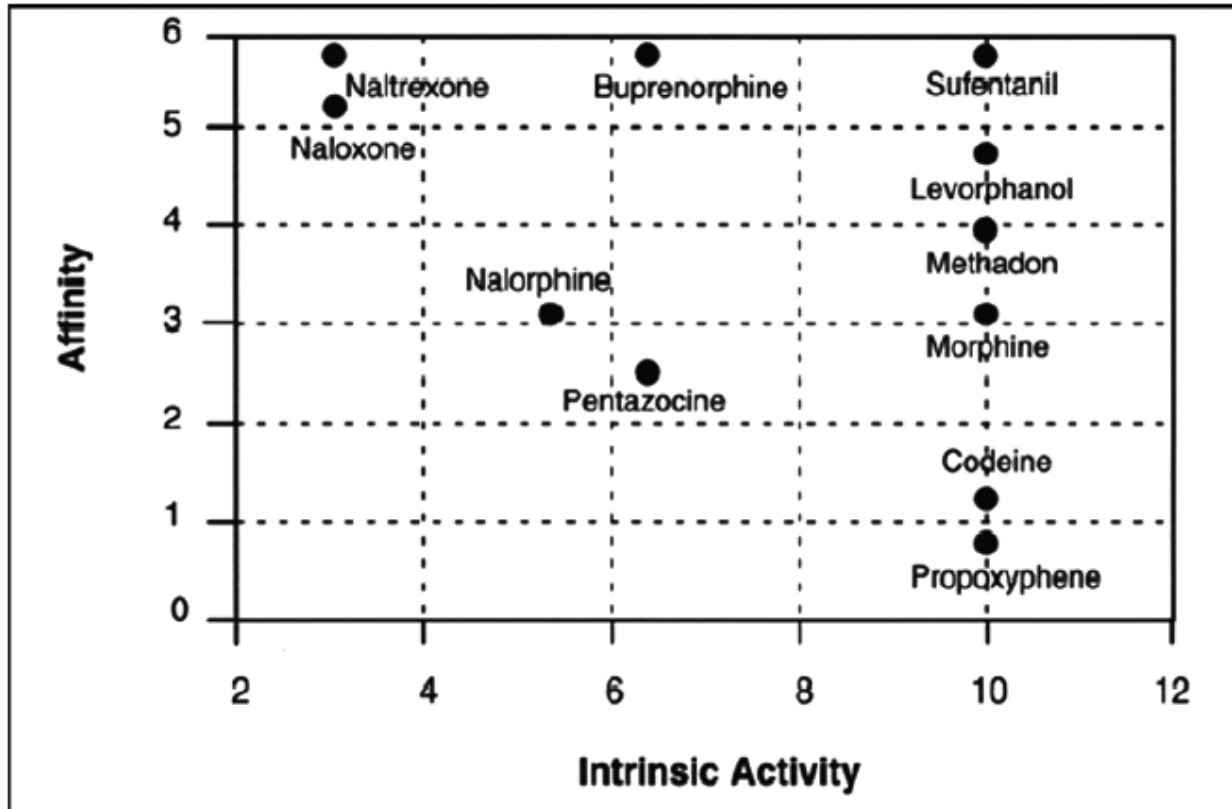
Lecture Outline

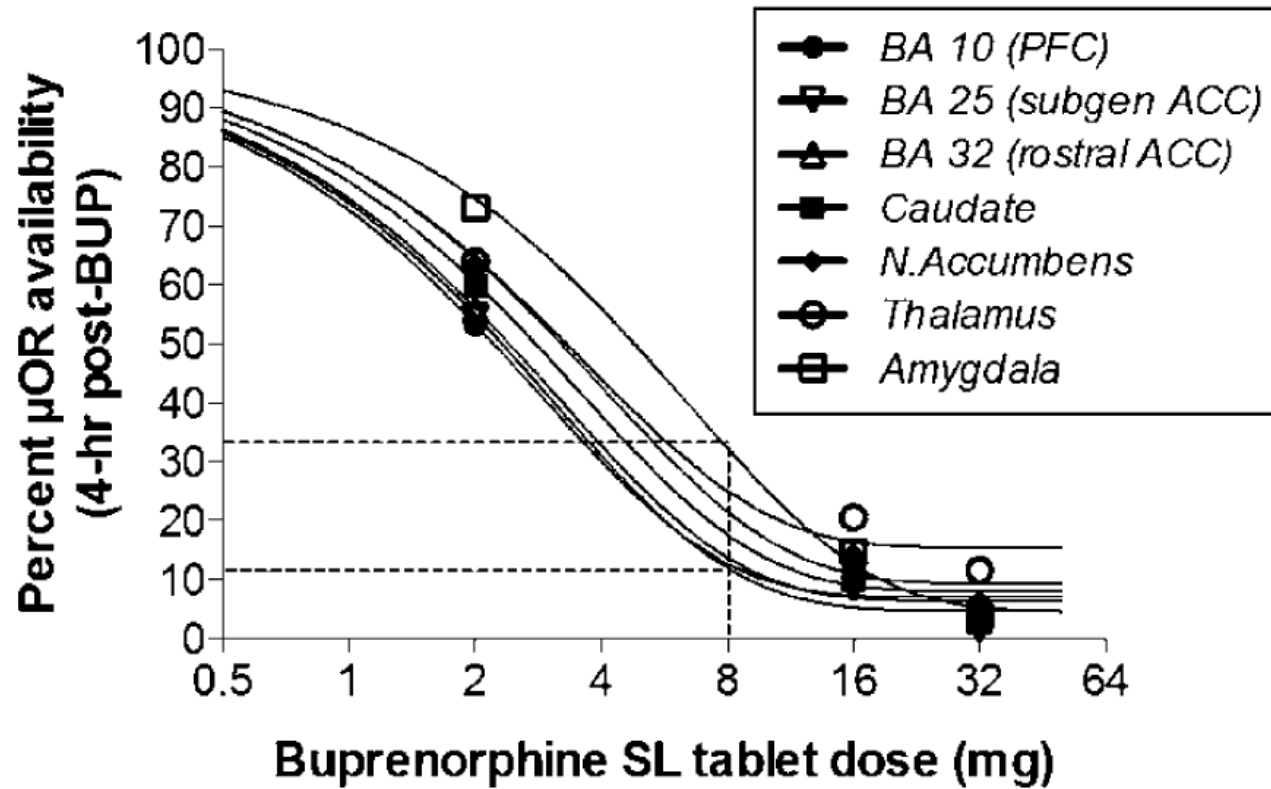
- Pharmacology
- Her Suboxone is just trading one addiction for another
- He should have been off Suboxone a long time ago
- She doesn't need any pain meds for that injury because she takes Suboxone

Pharmacology

Hierarchy of Goals

1. Withdrawal suppression
2. Reduce illicit opioid use
3. Improve quality of life





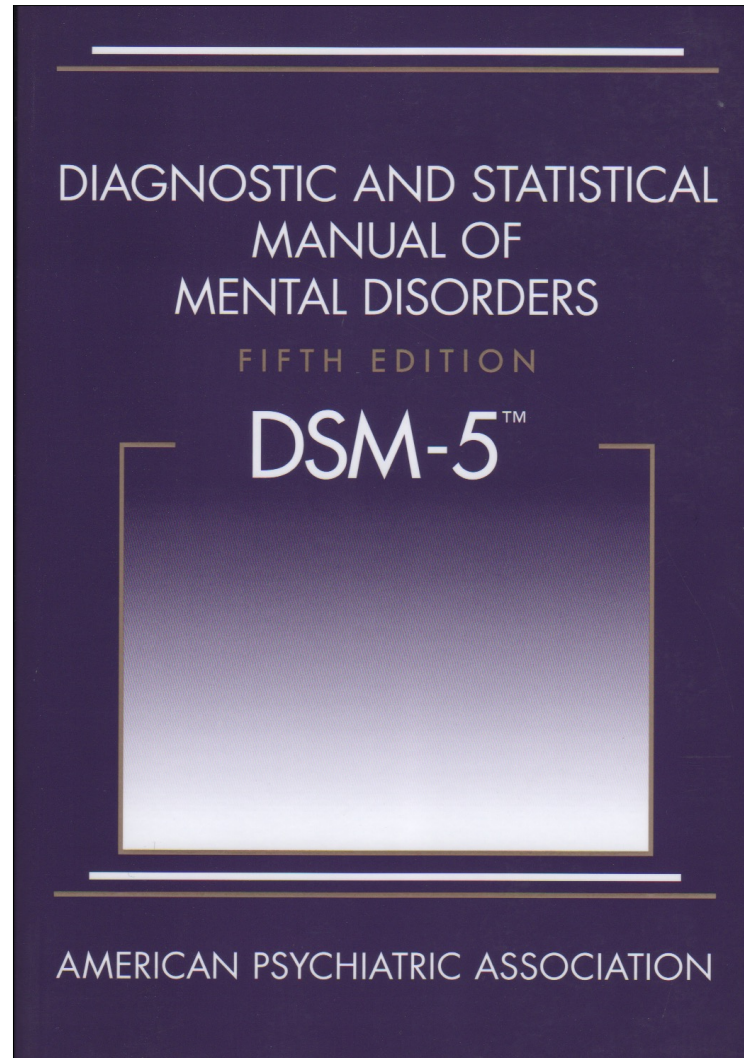
Trading Addictions

Myth #1

- Taking buprenorphine is just trading one addiction for another

Fact #1

- Patients who take buprenorphine generally do not meet diagnostic criteria Opioid Use Disorder
- Buprenorphine is usually adaptive
 - Promotes wellbeing (relieves distress)
 - Improves/restores function (reduces impairment)



Arlington, VA: American Psychiatric Association, 2013

DAVID *f*RENZ MD
MENTAL HEALTH & ADDICTION CARE

Opioid Use Disorder | 1

“ A problematic pattern of opioid use leading to clinically significant impairment or distress, as manifested by at least two of the following, occurring within a 12-month period ”

Opioid Use Disorder | 2

1. Opioids are often taken in larger amounts or over a longer period than was intended
2. There is a persistent desire or unsuccessful efforts to cut down or control opioid use
3. A great deal of time is spent in activities necessary to obtain the opioid, use the opioid, or recover from its effects
4. Craving, or a strong desire or urge to use opioids
5. Recurrent opioid use resulting in a failure to fulfill major role obligations at work, school, or home

Opioid Use Disorder | 3

6. Continued opioid use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of opioids
7. Important social, occupational, or recreational activities are given up or reduced because of opioid use
8. Recurrent opioid use in situations in which it is physically hazardous
9. Continued opioid use despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance

Opioid Use Disorder | 4

10. Tolerance

- This criterion is not considered to be met for those taking opioids solely under appropriate medical supervision

11. Withdrawal

- This criterion is not considered to be met for those individuals taking opioids solely under appropriate medical supervision

Old School

“ A maladaptive pattern of opioid use, leading to clinically significant impairment or distress ”



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Review

Quality of life among opiate-dependent individuals: A review of the literature

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ABSTRACT

Quality of life (QoL) has become an important outcome indicator in health care evaluation. A clear distinction has to be made between QoL – focussing on individuals' subjective satisfaction with life as a whole and different life domains – and health-related QoL (HRQoL), which refers to the absence of pathology. As opiate dependence is the primary drug of most persons entering treatment and as the attention for QoL in addiction research is growing, this review of the literature intends to summarise and differentiate the available information on QoL in opiate-dependent individuals. A comprehensive literature review was conducted, including database searches in Web of Science, PubMed and Cochrane Database of Systematic Reviews. Articles were eligible for review if they assessed QoL or HRQoL of opiate-dependent individuals, used a QoL or HRQoL instrument and reported at least one specific outcome on QoL or HRQoL. In total, 38 articles have been selected. The review showed that various instruments ($n = 15$) were used to measure QoL, mostly HRQoL instruments. Opiate-dependent individuals report low HRQoL compared with the general population and people with various medical illnesses. Generally, participation in substitution treatment had a positive effect on individuals' HRQoL, but long-term effects remain unclear. Psychological problems, older age and excessive alcohol use seem to be related with lower HRQoL scores. The assessment of QoL in research on opiate dependence is still in its infancy. Still, the chronic nature of drug use problems creates the necessity to look at outcomes beyond the direct consequences of drug dependence and based on clients' needs. HRQoL, with its unilateral focus on the functional status of clients, does not give information on clients' own experiences about the goodness of life, and is as a consequence unsuitable for measuring QoL. Future research starting from a subjective, multidimensional approach of the concept of QoL is required.

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Introduction

Quality of life and health-related QoL: two different constructs

Patients' self-reported outcomes (e.g. quality of life) have become an increasingly important source of information in health care. This has been helped by a focus on the empowerment of help-seeking individuals (Segal, 1998) and the prevalence of various chronic illnesses (Guyatt et al., 2007; Smith, Avis, & Assmann, 1999). The limited curing effect of treatment services for chronic diseases such as diabetes and depression, for example, has created the need for long-term treatment and a shift from cure to care, with attention to the patients' perspectives (Wiklund, 2004).

The best known patient-reported outcome is quality of life (QoL) (Valderas et al., 2008; Winklbauer, Jagsch, Ebner, Thau, & Fischer, 2008). During the last decades various disciplines have focused on QoL (Bowling & Brazier, 1995), however, the concept is vague and its use inconsistent (Dijkers, 2007; Farquhar, 1995; Skevington,

Lofy, & O'Connell, 2004; Smith et al., 1999). Researchers often consider terms like "health status" and "health-related quality of life" (HRQoL) as synonymous with QoL (Muldoon, Barger, Flory, & Manuck, 1998), resulting in the inconsistent use of the concept (Gill, Alvan, & Feinstein, 1994). HRQoL has its foundations in a definition of health from 1947 (Cummins, Lau, & Stokes, 2004) and this contrasts sharply with subjective well-being or subjective QoL. It measures the effects of a disease on individuals' everyday functioning, with special attention given to physical and psychological limitations (Burgess et al., 2000). HRQoL is frequently used in general medicine to demonstrate the absence of pathology. In social sciences and psychiatry, on the other hand, there is a strong focus on respondents' reported satisfaction with life as a whole, including a multidimensional or holistic approach to the concept of QoL (Cummins et al., 2004; Van Nieuwenhuizen, Schone, & Koeter, 2002). Several authors (Katschube, 2006; Scholick & Verdugo Alonso, 2002) have demonstrated the importance of individuals' own perceptions in conceptualizing QoL and approach QoL as a "sensitising concept" – starting from individuals' subjective experiences – rather than as a definite construct with a fixed definition. Consequently, we will make a distinction here between HRQoL and subjective QoL and indicate how Quality of Life was

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Clinical Improvement

- “ Participation in substitution treatment seemed to have a positive effect on individuals’ (HR)QoL [health-related quality of life]
- “ Improvements on various life domains—including (HR)QoL and subjective QoL—were most obvious during the first months of treatment
- “ The observed improvements persisted over a long-term period... ”

Pressure to Taper Off

Myth #2

- Patients shouldn't take Suboxone indefinitely and need to get off it

Fact #2

- Patients with opioid addiction generally do poorly after they taper off of opioids, including buprenorphine
- A century of literature demonstrates a high rate of relapse and negative health consequences including excess mortality

amount of laryngeal manipulation. A good light was thrown upon the operating field, and thereby the entire condition thoroughly explored before any operative procedure was undertaken. A 20 per cent. solution of cocaine was sprayed over the pharynx, post-pharyngeal wall, soft palate and larynx, in order to produce a complete anesthesia of the entire surrounding localities. A gag was inserted on the left side of the mouth. This instrument should be made use of in all such operative manoeuvres, so that one may be able to control the opening of the mouth, and not trust to the patient. An assistant should control the head of the patient against an ordinary head rest. These are the preliminary steps that I generally pursue.

The cutting was done with Lennox Brown's laryngeal dilator with cutting blades. This instrument possesses these advantages over the Whistler cutting dilator: In passing tubes into the larynx many difficulties are encountered, and especially through a cicatricial stricture are much greater than generally stated. This instrument of Lennox Brown's possesses the advantage of being a hollow tube of Schrötter and the cutting dilator of Whistler, so that the surgeon in operating is always sure by the outward passage of air, when the hollow tube is in the larynx, is able to incise with more certainty as to what he is cutting and, moreover, in case of spasm the air passages are not entirely obstructed. A large size laryngeal mirror is necessary in order to procure a good laryngeal image. The Lennox Brown cutting dilator was introduced with ease and the cicatricial web cut through. The breathing during the introduction of this instrument was momentarily disturbed, after its complete passage normal breathing was carried on through the hollow opening in the dilator. Hæmorrhage was very slight. After the incision the instrument was withdrawn and the larynx thoroughly sprayed out. A few minutes later a large-size hard rubber intubation tube was introduced into the larynx and kept there for three days without its removal. Cold applications by means of compresses were used for forty-eight hours with irrigation of the larynx, also spraying with a 10 per cent. solution of cocaine for the relief of pain; this was continued for two days with much relief to the patient. Iodide of potash was again resorted to. Three days later the tube was removed and again replaced. An examination after the first removal of the tube showed a great improvement and healing of the wounded cicatricial web. The cicatrix was diminished, and the size of the opening made by the incision was thus kept open by the continued dilatation of the larger sized tubes, until the edges of the cicatricial tissue were well healed. The time of healing of these edges lasted seven days. The tubes should be worn for two weeks at least after their first introduction. The tube should be removed daily for

cleansing. Astringent solutions should be used in spray form for after-treatment. This patient made a complete recovery as the result of this operation. It is now two months since the tube has been permanently removed, and when I last examined the larynx I found the cicatricial web in the same state as after the incision. The patient was in excellent condition and breathing at a normal rate.

This method of treatment seems to me to be of a permanent value as compared with other methods. There is no necessity for a preliminary tracheotomy. The tedious dilatation with dilating instruments for an indefinite length of time, and then with a view of a non success.

I do not mean to say that every case can thus be treated, but there are cases which come under our notice for treatment where such treatment by this mode I here introduce deserves a trial.

I have used these modes of operating in many such cases which are too numerous to describe here. These two cases by way of illustrating which have just above described and are sufficient to bring before you what can still be expected of intubation of the larynx in connection with other operations.

83 2d Avenue, New York City.

TREATMENT OF MORPHINE HABIT.

BY EMORY LANPHEAR, M.D.,
OF KANSAS CITY, MO.,
SURGEON TO EAST SIDE DISPENSARY.

By the introduction of new remedies considerable change has taken place during the past three years in the management of cases of the morphine habit. My present method of treating is, briefly, this: Upon admission to the hospital the patient is introduced to his special nurse who is to be his constant companion during the succeeding six weeks, and after being made comfortable is given an initiatory bath. He is then requested to give up his instruments and morphine as the physician henceforth is to attend to the administration of the drug; he does this willingly and makes no attempt to concealment if he be in earnest about undergoing treatment—if he be not, cure were better left unattempted. Under no circumstances is the patient humiliated by searching the clothing and trunk, as advised by many authors—it is the keynote of dissatisfaction and discord can be the only result; in other words the subject is made to feel that confidence between patient and physician is mutual.

WITHDRAWAL.

After these preliminary steps an assurance is given the patient that he is to be made as comfortable as possible and that the pain will be reduced to the minimum. He is then left to become accustomed to his surroundings, and at the

sixteenth day the child, usually quiet and of an amiable disposition, was nervous and fretful, evincing a sense of apprehension, a decided loss of appetite; moreover he drank water with some difficulty. A day or so later the reflex irritability of the deglutitory apparatus became so marked that the child realized that water could not be drunk without causing a most distressing spasm. Despite this fact he made repeated efforts to satisfy his thirst until within a day or two the spasms were so violent that the patient not only was unable to drink, but he evinced the dislike of water characteristic of hydrophobia. On the nineteenth day the first symptom of paralysis appeared; the gait was unsteady and staggering. The paralysis became marked on the twentieth day. This stage of the disease lasted but twelve hours, however, an unusually short duration. During this stage of the disease the facial symptoms, expressions of fear, or apprehension of impending danger, became aggravated.

During this stage the child developed twitchings of the extremities—there had been only a slight tremor of the hands before—and he suffered from hallucinations which frightened him; at times, however, he seemed to imagine that he was driving horses, making a peculiar frequent clucking sound, or he would call to dogs—spontaneous images of his life on a farm. At this time chloral and morphia were administered with quieting effects. The temperature rose to 107.2 F. and there was a marked tendency to sweating. The tongue was heavily coated, and on several occasions he vomited a thick, yellowish, creamy fluid. There was considerable drooling and collection of saliva owing to the inability to swallow. When the mouth was not kept free from saliva by frequent swabbing, the patient, breathing through the mouth, caused the characteristic frothing. This condition was particularly pronounced during the convulsive stages, owing to the increased rapid respirations. These tonic convulsions, particularly of the lower limbs, occurred from fifteen to twenty minutes apart; in the intervals between these the patient ground his teeth and muttered continuously. In the meantime the eyes became red and glassy; the pupils were widely dilated; the lower jaw dropped and the patient breathed with a respiratory grunt. About two hours before death there was marked cyanosis, the eyes became fixed in a vacant stare and consciousness was lost. At this time the muscles became flaccid and death resulted from paralysis of the respiratory muscles.

MORPHINISM AND ITS TREATMENT

ERNEST S. BISHOP, M.D.
NEW YORK

Every physician is familiar with at least a few cases of morphinism. Nearly every physician has made effort to rescue from the addiction its victim, and as a rule has given over the effort as hopeless, because even when the patient has been taken off his drug, he relapsed, or while under treatment he did not have the courage to persevere or the stamina to endure the necessary suffering. The profession as a whole has adopted a cynical attitude toward the possibility of permanent cure and many have relegated to quacks and charlatans the treatment which these poor people seek.

Three lines of endeavor have been employed: so-called slow reduction, sudden withdrawal and withdrawal accompanied by the administration of belladonna or its alkaloids.

"Slow reduction" simply means gradually reducing the patient's accustomed dosage. It is perfectly easy and unnecessarily slow up to the point of minimum organic need. Then must come withdrawal, and the wrench of actual final withdrawal is nearly as severe from a very small dosage as from a moderate one. Prolonging its accomplishment means subjecting the patient to the strain of persistent craving, discomfort, self-

denial and organic need. These sequelae or remnants of the old trouble remain for months and render the patient especially prone to relapse.

As to sudden withdrawal, anyone who has watched a addict in the agonies of morphia deprivation will hesitate to attempt to prolong this to convalescence. Those who have undergone it show for years, in shattered nerves, premature age, etc., the effects of the terrific shock.

It has been shown from studies of the blood of patients undergoing very slow and very rapid withdrawal that they have, following treatment, very much lowered vitality and powers of recuperation. This is the natural result of the prolonged, nagging strain of the one and the shock of the other.

Withdrawal by the use of belladonna or its alkaloids has been attempted for a long time and in many combinations, and has a rational basis. The clinical picture of full belladonna effect is in many ways similar to that of an acute febrile disturbance. Morphia users are much less susceptible to such febrile attacks than ordinary men. During an attack, however, they are perfectly comfortable on a dosage far below that to which they are accustomed. The same is true of full belladonna-effect. Whatever its mode of action, whether it simply benumbs sensation, or produces artificially the systemic disturbance of a febrile condition, or is actually physiologically antidotal to morphia and other narcotics, it does reduce craving in the narcotic addict.

In my work in the alcoholic service of Bellevue Hospital, I had to treat many cases of morphia addiction. Attempts at slow withdrawal proved wearisome, difficult, and unsatisfactory in application and abortive in results. The patients could not be kept a sufficient time in the hospital, and could not afford to retire to sanatoriums for the months of prolonged convalescence necessary to enable them to return to active life with its strain and manifold temptations without a certainty of relapse. Early trials of the treatment, an outline of which was published by Dr. Alexander Lambert, were unsatisfactory in my hands. Although some patients came through well and comfortably, too many others did so with too much suffering and too severe and persistent prostration and other sequelae. This was due to my inexperience and lack of understanding of morphia cases.

Subsequent observation showed three things.

1. A morphia addict can take enormous single doses without any untoward effect.
2. The duration of his freedom from craving following his dose is in ratio to the amount taken and can be fairly estimated.
3. Following adequate catharsis, smaller amounts of the drug are needed than before.

It seemed to me, therefore, that some method based on these facts and employing belladonna could best accomplish the result. That described by Dr. Lambert met these requirements. It had given unclouded results, and I determined to try it again, in the light of further experience, endeavoring to study the occasion for its failure in the hands of so many, including myself, and to minimize the difficulties with which it had been attended in the hands of everybody.

Analysis of cases and of results obtained during and following treatment points to a conclusion that the fairly robust individual not using excessive amounts of the drug, and with good resistance and reactive ability, responds well and goes through this method of rapid withdrawal with but little complicating disturbance or sequelae. On the other hand, the poorly nourished,

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Relapse

“ Nearly every physician has made effort to rescue from the addiction its victim, and as a rule has given over the effort as hopeless, because even when the patient has been taken off his drug, he relapsed... ”

A FOLLOW-UP OF NARCOTIC ADDICTS Mortality, Relapse and Abstinence*

JOHN A. O'DONNELL, Ph.D.

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Kentucky residents who were treated for narcotic addiction at the U. S. Public Health Service Hospital, Lexington, Kentucky, between May, 1935 and December, 1959, were followed to determine what happened to them after discharge. Sample size was 266. More than half had died. Of living subjects, more than half were abstinent from narcotics when located.

THIS PAPER is a report on part of the data obtained by a follow-up study of patients treated for narcotic addiction in the Lexington Hospital who had been residents of Kentucky at the time of first admission. Sample size was 266 subjects, all white. Selection was done by stratified random sampling of counties.

Generalizations from findings on this sample are, strictly speaking, permissible only to Kentucky residents treated at Lexington. For practical purposes findings probably also apply to white patients from the southern states. It would not be legitimate, however, to generalize from these findings to the addict popula-

tion today, and specifically not to the addicts from metropolitan areas who are the bulk of that population.

The sample includes subjects admitted to the hospital as early as 1935, when the hospital opened, and as late as 1959 provided there had been at least one discharge from the hospital before the end of 1959. Field work began in March, 1961, and ended October 15, 1963. This report is restricted to the mortality in the sample, and to some findings on the addiction status of the living subjects.

One-hundred and forty-four of the 266 sample subjects had died before they could be located. Six more of those who were interviewed died later, before

*Presented at the 1964 Annual Meeting; accepted for publication, June 11, 1964.

This paper was first presented to the Committee on Drug Addiction and Narcotics, National Academy of Sciences—National Research Councils, February, 1964. The study was supported by a National Institutes of Health Grant, M4014.

Readmission Rates at Lexington Hospital for 43,215 Narcotic Drug Addicts

JOHN C. BALL, Ph.D., WILLIAM O. THOMPSON, Ph.D., and DAVID M. ALLEN, Ph.D.

A STUDY of rates of readmission of patients to the Public Health Service Hospital, Lexington, Ky., during a 32-year period was undertaken to analyze the association of specific demographic and treatment variables with repeated hospitalization of opiate addiction. In the present context, rates of readmission are seen as providing an index of relapse within the various patient populations and a means of assessing the efficacy of treatment.

The first addicts were admitted to the hospital at Lexington on May 28, 1935 (1). From that date to the end of 1966, 43,215 addicts were admitted for psychiatric and medical treatment. Inasmuch as many of these patients relapsed to abuse of drugs and returned for further treatment, the recorded number of admissions to the hospital is considerably greater than the number of patients; during the 32 years there were 77,076 admissions.

Computerized Enumeration Procedure

Admission and discharge information pertaining to all addicts treated at the Lexington hospital since 1935 was retrieved and computerized. After this data bank was established (during a 3-year period), it became possible to analyze hospital and demographic variables concerning the total hospital population of 43,215 patients. Indeed, until the master file was established it was not possible even to count the number of patients admitted.

Of the 43,215 addicts hospitalized at Lexington, 70 percent were voluntary patients and

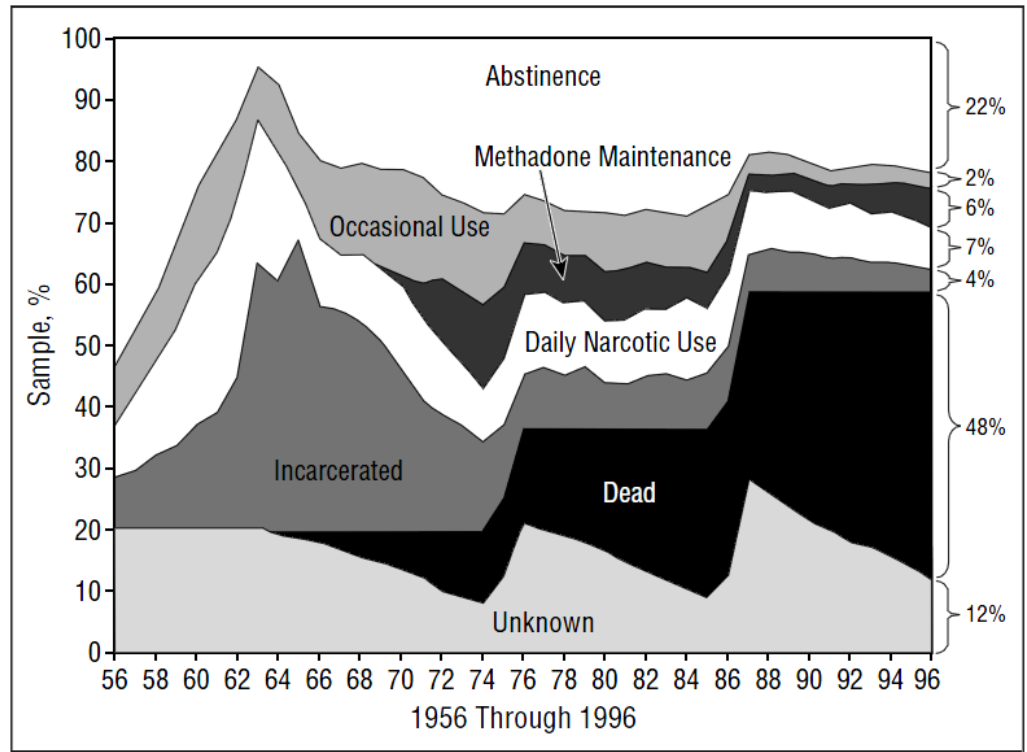
30 percent were Federal prisoners. The voluntary patients could, at their discretion, leave the institution at any time after admittance and, in fact, most did leave against medical advice (2). Notwithstanding their early discharge, many patients returned for further treatment. Thus, free and confidential treatment for drug abuse was continually available to addicts during this 32-year period (3).

In addition to the voluntary patients, Federal prisoners were also admitted to the Lexington hospital. These prisoners were serving designated sentences and were not free to leave; they could, however, be subsequently readmitted as either prisoners or voluntary patients.

Admission Trends, 1935-66

From 1935 to 1938, the Lexington hospital accepted only male patients from throughout the United States. After 1938, when a second Public Health Service Hospital was opened at Fort Worth, Tex., the Lexington hospital had the eastern part of the nation as its principal catchment area. Since July 16, 1941, female addicts from the entire United States have been admitted to the Lexington hospital. The subsequent analysis refers only to data for the Lexington hospital.

Dr. Ball is a professor, department of psychiatry, Temple University Health Sciences Center, Philadelphia. Dr. Thompson and Dr. Allen are assistant professors, department of statistics, University of Kentucky, Lexington.



The natural history of narcotics addiction among a male sample (N=581).

A Medical Treatment for Diacetylmorphine (Heroin) Addiction

A Clinical Trial With Methadone Hydrochloride

Vincent P. Dole, MD, and Marie Nyswander, MD

A group of 22 patients, previously addicted to diacetylmorphine (heroin), have been stabilized with oral methadone hydrochloride. This medication appears to have two useful effects: (1) relief of narcotic hunger, and (2) induction of sufficient tolerance to block the euphoric effect of an average illegal dose of diacetylmorphine. With this medication, and a comprehensive program of rehabilitation, patients have shown marked improvement; they have returned to school, obtained jobs, and have become reconciled with their families. Medical and psychometric tests have disclosed no signs of toxicity, apart from constipation. This treatment requires careful medical supervision and many social services. In our opinion, both the medication and the supporting program are essential.

The question of "maintenance treatment" of addicts is one that is often argued but seldom clearly defined. If this procedure is conceived as no more than an unsupervised distribution of narcotic drugs to addicts for self-administration of doses and at times of their choosing, then few physicians could accept it as proper medical practice. An uncontrolled supply of drugs would trap confirmed addicts in a closed world of drug taking, and tend to spread addiction. This procedure certainly would not qualify as "maintenance" in a medical sense. Uncontrolled distribution is mentioned here only to reject it, and to emphasize the distinction between distribution and medical prescription. The question at issue in the present study was whether a narcotic medicine, prescribed by physicians as part of a treatment program, could help in the return of addict patients to normal society.

No definitive study of medical maintenance has yet been reported. The Council on Mental Health of the American Medical Association, after a thor-

ough review of evidence available in 1957,¹ concluded that "The advisability of establishing clinics or some equivalent system to dispense opiates to addicts cannot be settled on the basis of objective facts. Any position taken is necessarily based in part on opinion, and on this question opinions are divided." With respect to previous trials of maintenance treatment, the Council found that "Assessment of the operations of the narcotic dispensaries between 1919 and 1923 is difficult because of the paucity of published material. Much of the small amount of data that is available is not sufficiently objective to be of great value in formulating any clear-cut opinion of the purpose of the clinics, the way in which they operated, or the results attained." No new studies bearing on the question of maintenance treatment have appeared in the eight years since this report was published. Meanwhile, various medical and legal committees have called for additional research."²

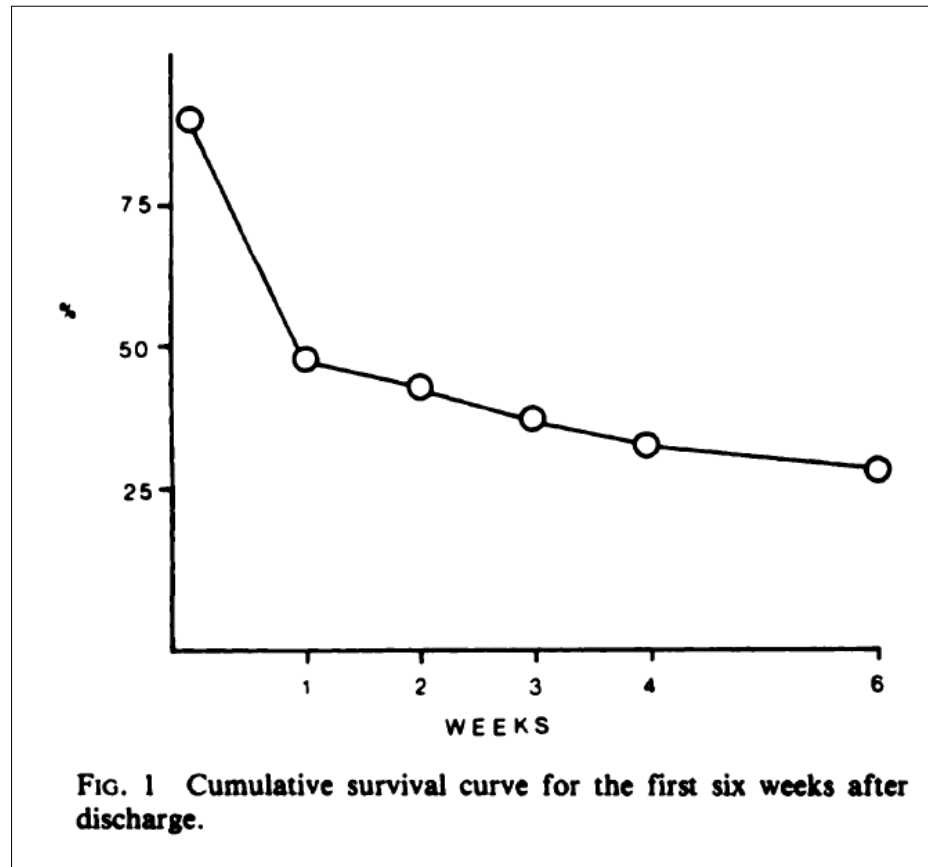
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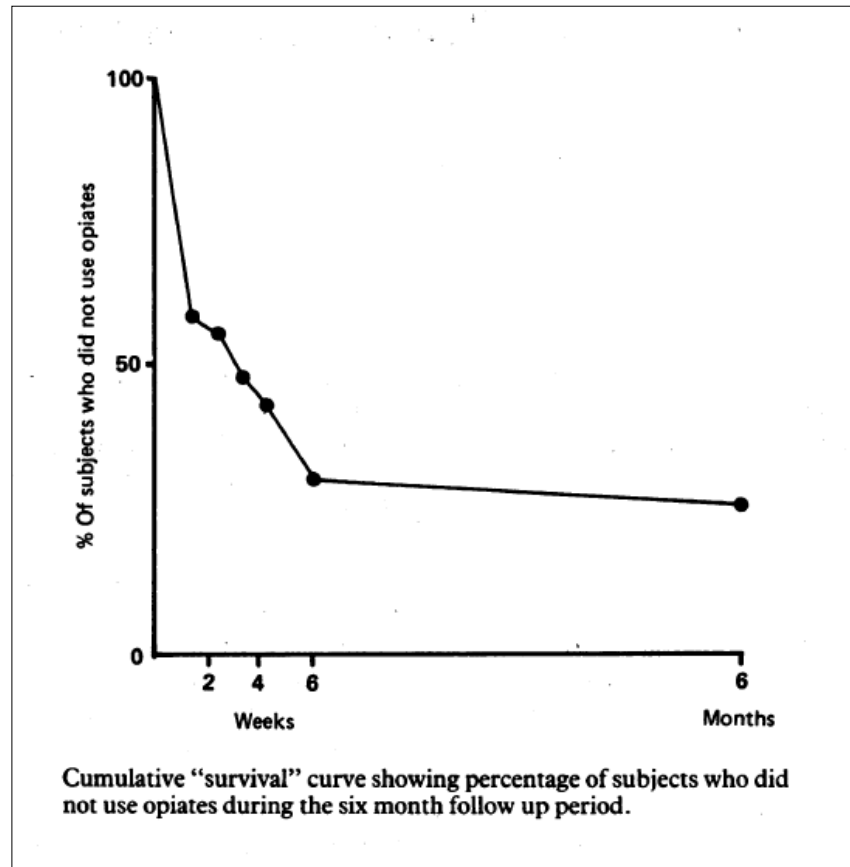
The present study, conducted under the auspices of the departments of health and hospitals, New York city, has yielded encouraging results; patients who before treatment appeared hopelessly addicted are now engaged in useful occupations and are not using diacetylmorphine (heroin). As measured by social performance, these patients have ceased to be addicts. It must be emphasized that this paper is only a progress report, based on treatment of 22 patients for periods of 1 to 15 months. Such limited study obviously does not establish a new treatment for general application. The results, however, appear sufficiently promising to justify further trial of the procedure on a larger scale.

Procedure

The patients admitted to the program to date were men, aged 19 to 37, "mainline" diacetylmorphine users for several years with history of failures

From the Rockefeller Institute, and Manhattan General Division of Beth Israel Hospital, New York.
Reprint requests to Rockefeller Institute, New York 10021 (Dr. Dole).





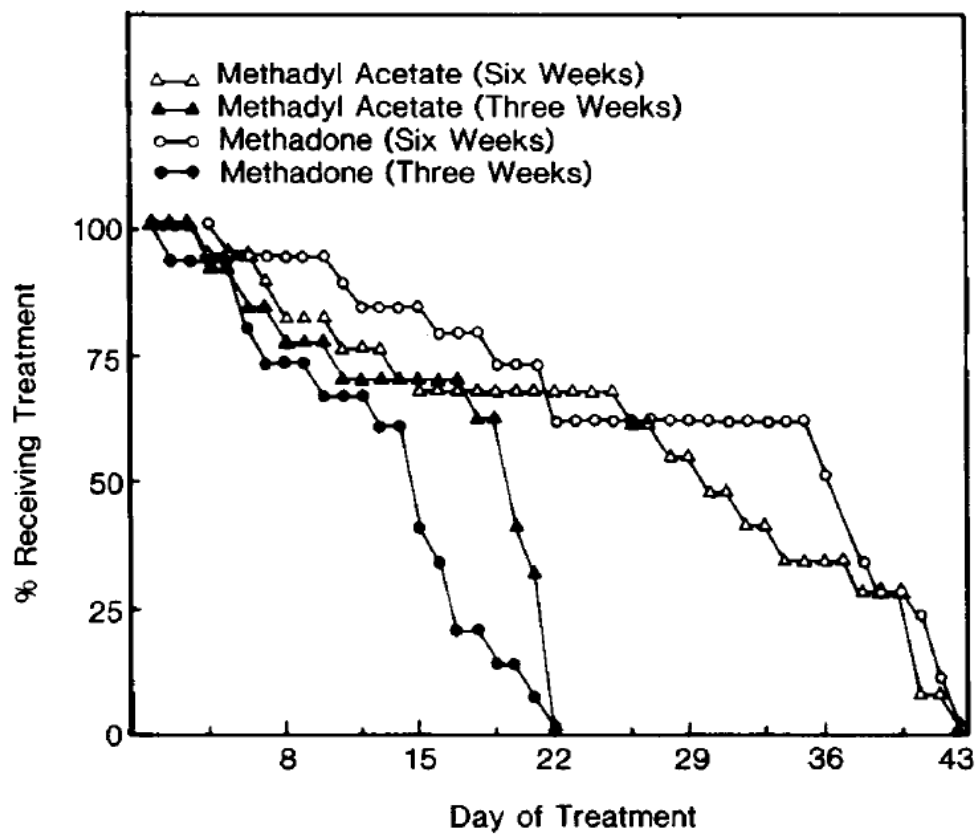
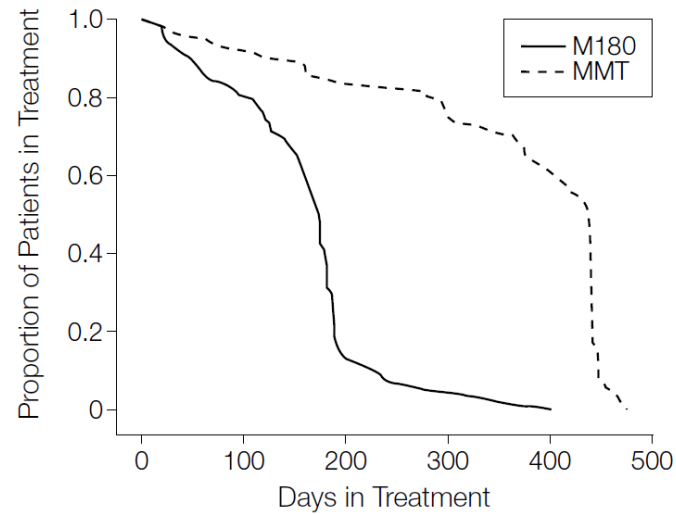


Fig 2.—Retention in treatment in each experimental group.

Figure 3. Survival Function by Treatment Group



Proportion of study participants in treatment by group over time. M180 indicates 180-day methadone-assisted detoxification; MMT, methadone maintenance treatment. For significant differences between conditions, Wilcoxon $\chi^2_1, 85.0$ ($P < .001$).

Leaving Methadone Treatment: Lessons Learned, Lessons Forgotten, Lessons Ignored

STEPHAN MAGURA, PH.D., AND ANDREW ROSENBLUM, PH.D.

Abstract

Despite the demonstrated benefits of methadone maintenance, there have been concerns about the ethics, necessity and expense of maintaining addicts on methadone indefinitely. The inability of many patients to achieve normative levels of psychosocial functioning with methadone, combined with widely held attitudes favoring drug abstinence over replacement medication, has led to attempts to promote time-limited methadone treatment. This paper reviews the published research literature on post-discharge outcomes of patients exiting from extended methadone detoxification, "abstinence-oriented" methadone programs, and regular methadone maintenance programs. Virtually all of these studies document high rates of relapse to opioid use after methadone treatment is discontinued. Most of the patients studied left treatment without meeting clinical criteria for detoxification, although high relapse rates were also reported for patients who completed this program. The detrimental consequences of leaving methadone treatment are dramatically indicated by greatly increased death rates following discharge. Until more is learned about how to improve post-detoxification outcomes for methadone patients, treatment providers and regulatory/funding agencies should be very cautious about imposing disincentives and structural barriers that discourage or impede long-term opiate replacement therapy.

Key Words: Methadone maintenance, drug abstinence, post-discharge outcomes.

Introduction

PREVIOUS RESEARCH HAS SHOWN that outcomes have generally been poor after short-term heroin/opiate detoxification; large percentages of detoxified addicts rapidly relapse to heroin/opiate use (1). The availability of naltrexone, an opiate antagonist, to extend opiate abstinence after detoxification has not altered this verdict; few persons to whom naltrexone was administered continue to take it for more than a month or two (2, 3). However, methadone maintenance with adequate dosing (4, 5) has been shown to eliminate or dramatically reduce patients' heroin use and improve their psychosocial functioning (6-9).

Nevertheless, even from the outset, there have been concerns about the ethics, wisdom, necessity and expense of maintaining addicts on

an opiate replacement indefinitely, possibly for the rest of their lives (10, 11). The depiction of irreversible neurological and metabolic changes in long-term opiate addicts remains a credible hypothesis, not acceptable by all, to help explain the remarkable persistence of opiate misuse by individuals (12). If methadone-maintained patients generally achieved a normative level of psychosocial functioning, surely there would be less criticism of the modality, but this goal has not been achieved. Addicts usually improve substantially after entering methadone treatment, particularly by eliminating or reducing opiate use, drug-injection-related health risk habits and criminal activity. However, they often continue to misuse substances other than opioids (a pattern usually pre-dating treatment) and most remain economically dependent. An excellent comprehensive review of methadone treatment issues can be found in Ward et al. (9).

The mixed outcomes of methadone maintenance, at least as it is traditionally administered and delivered, have led to a curious conclusion in some quarters. Because many patients remain economically dependent,

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Discussion

Outcome data reported for more than 30 methadone discharge studies reviewed in this paper lead to three main conclusions: (a) most patients who left methadone treatment were not identified by their clinic as therapeutically ready for discharge; (b) among patients who began a therapeutically planned discharge, most left methadone treatment before completing their detoxification; and (c) among patients who completed a therapeutically planned discharge, most relapsed to heroin use.

ONLINE FIRST

Adjunctive Counseling During Brief and Extended Buprenorphine-Naloxone Treatment for Prescription Opioid Dependence

A 2-Phase Randomized Controlled Trial

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Context: No randomized trials have examined treatments for prescription opioid dependence, despite its increasing prevalence.

Objective: To evaluate the efficacy of brief and extended buprenorphine hydrochloride–naloxone hydrochloride treatment, with different counseling intensities, for patients dependent on prescription opioids.

Design: Multisite, randomized clinical trial using a 2-phase adaptive treatment research design. Brief treatment (phase 1) included 2-week buprenorphine-naloxone stabilization, 2-week taper, and 8-week postmedication follow-up. Patients with successful opioid use outcomes exited the study; unsuccessful patients entered phase 2: extended (12-week) buprenorphine-naloxone treatment, 4-week taper, and 8-week postmedication follow-up.

Setting: Ten US sites.

Patients: A total of 653 treatment-seeking outpatients dependent on prescription opioids.

Interventions: In both phases, patients were randomized to standard medical management (SMM) or SMM plus opioid dependence counseling; all received buprenorphine-naloxone.

Main Outcome Measures: Predefined “successful outcome” in each phase: composite measures indicating minimal or no opioid use based on urine test–confirmed self-reports.

Results: During phase 1, only 6.6% (43 of 653) of patients had successful outcomes, with no difference between SMM and SMM plus opioid dependence counseling. In contrast, 49.2% (177 of 360) attained successful outcomes in phase 2 during extended buprenorphine-naloxone treatment (week 12), with no difference between counseling conditions. Success rates 8 weeks after completing the buprenorphine-naloxone taper (phase 2, week 24) dropped to 8.6% (31 of 360), again with no counseling difference. In secondary analyses, successful phase 2 outcomes were more common while taking buprenorphine-naloxone than 8 weeks after taper (49.2% [177 of 360] vs 8.6% [31 of 360], $P < .001$). Chronic pain did not affect opioid use outcomes; a history of ever using heroin was associated with lower phase 2 success rates while taking buprenorphine-naloxone.

Conclusions: Prescription opioid–dependent patients are most likely to reduce opioid use during buprenorphine-naloxone treatment; if tapered off buprenorphine-naloxone, even after 12 weeks of treatment, the likelihood of an unsuccessful outcome is high, even in patients receiving counseling in addition to SMM.

Trial Registration: clinicaltrials.gov Identifier: NCT00316277

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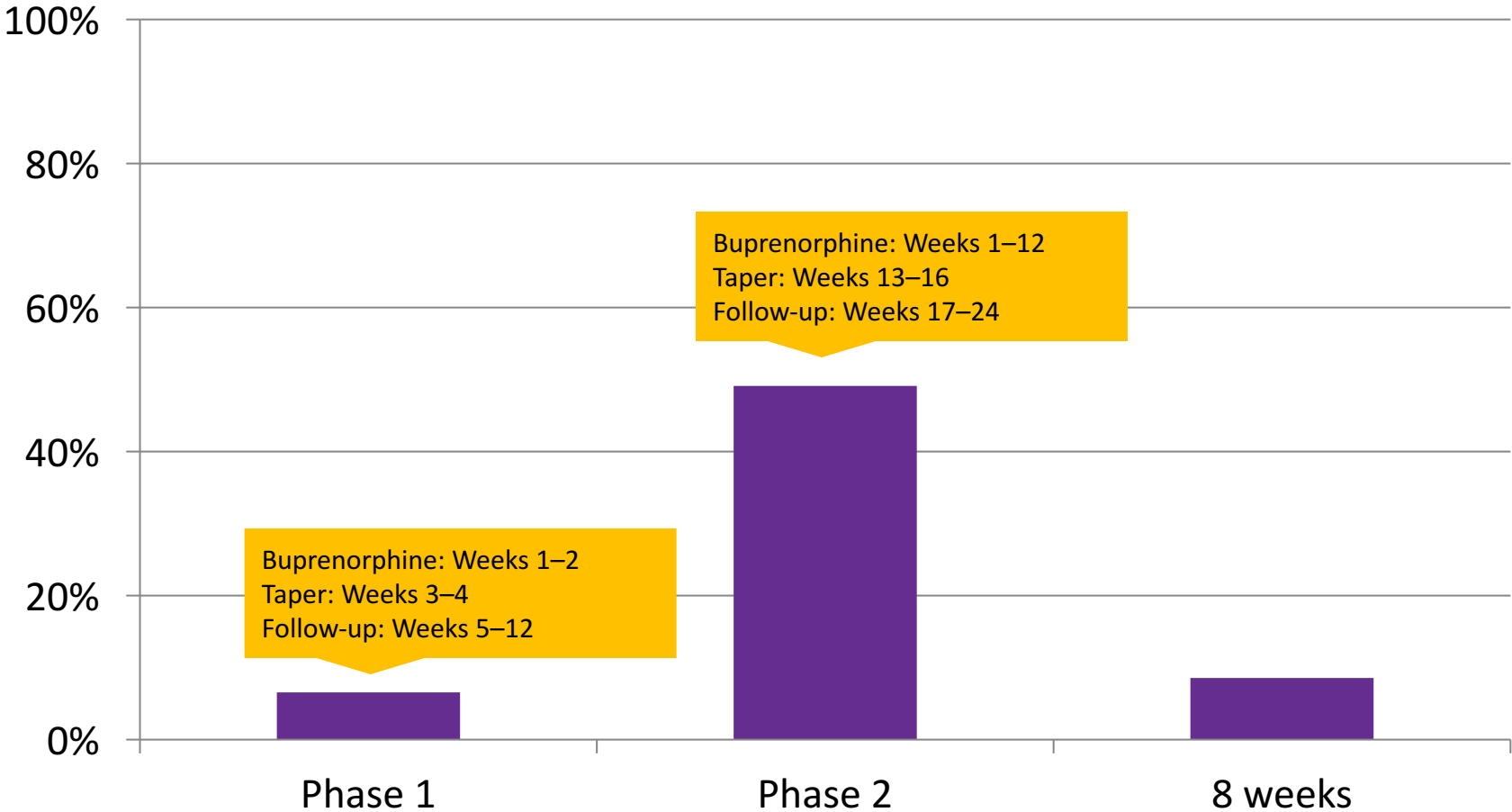
ABUSE OF PRESCRIPTION OPIOIDS is a significant public health and policy¹ concern, with increasing rates of nonmedical use,² emergency department visits,³ addiction treatment episodes,⁴ overdose deaths,⁵ and costs⁶

related to these drugs in recent years. Despite the growing prevalence of prescription opioid dependence and the availability and increasing use⁷ of buprenorphine hydrochloride treatment (primarily as buprenorphine hydrochloride–naloxone hydrochloride) in physician offices, most opi-

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Successful Opioid Use Outcome



Risk of death during and after opiate substitution treatment in primary care: prospective observational study in UK General Practice Research Database

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ABSTRACT

Objective To investigate the effect of opiate substitution treatment at the beginning and end of treatment and according to duration of treatment.

Design Prospective cohort study.

Setting UK General Practice Research Database

Participants Primary care patients with a diagnosis of substance misuse prescribed methadone or buprenorphine during 1990-2005. 5577 patients with 267 003 prescriptions for opiate substitution treatment followed-up (17732 years) until one year after the expiry of their last prescription, the date of death before this time had elapsed, or the date of transfer away from the practice.

Main outcome measures Mortality rates and rate ratios comparing periods in and out of treatment adjusted for sex, age, calendar year, and comorbidity; standardised mortality ratios comparing opiate users' mortality with general population mortality rates.

Results Crude mortality rates were 0.7 per 100 person years on opiate substitution treatment and 1.3 per 100 person years off treatment; standardised mortality ratios were 5.3 (95% confidence interval 4.0 to 6.8) on treatment and 10.9 (9.0 to 13.1) off treatment. Men using opiates had approximately twice the risk of death of women (mortality rate ratio 2.0, 1.4 to 2.9). In the first two weeks of opiate substitution treatment the crude mortality rate was 1.7 per 100 person years; 3.1 (1.5 to 6.6) times higher (after adjustment for sex, age group, calendar period, and comorbidity) than the rate during the rest of time on treatment. The crude mortality rate was 4.8 per 100 person years in weeks 1-2 after treatment stopped, 4.3 in weeks 3-4, and 0.95 during the rest of time off treatment: 9 (5.4 to 14.9), 8 (4.7 to 13.7), and 1.9 (1.3 to 2.8) times higher than the baseline risk of mortality during treatment. Opiate substitution treatment has a greater than 85% chance of reducing overall mortality among opiate users if the average duration approaches or exceeds 12 months.

Conclusions Clinicians and patients should be aware of the increased mortality risk at the start of opiate substitution treatment and immediately after stopping

treatment. Further research is needed to investigate the effect of average duration of opiate substitution treatment on drug related mortality.

INTRODUCTION

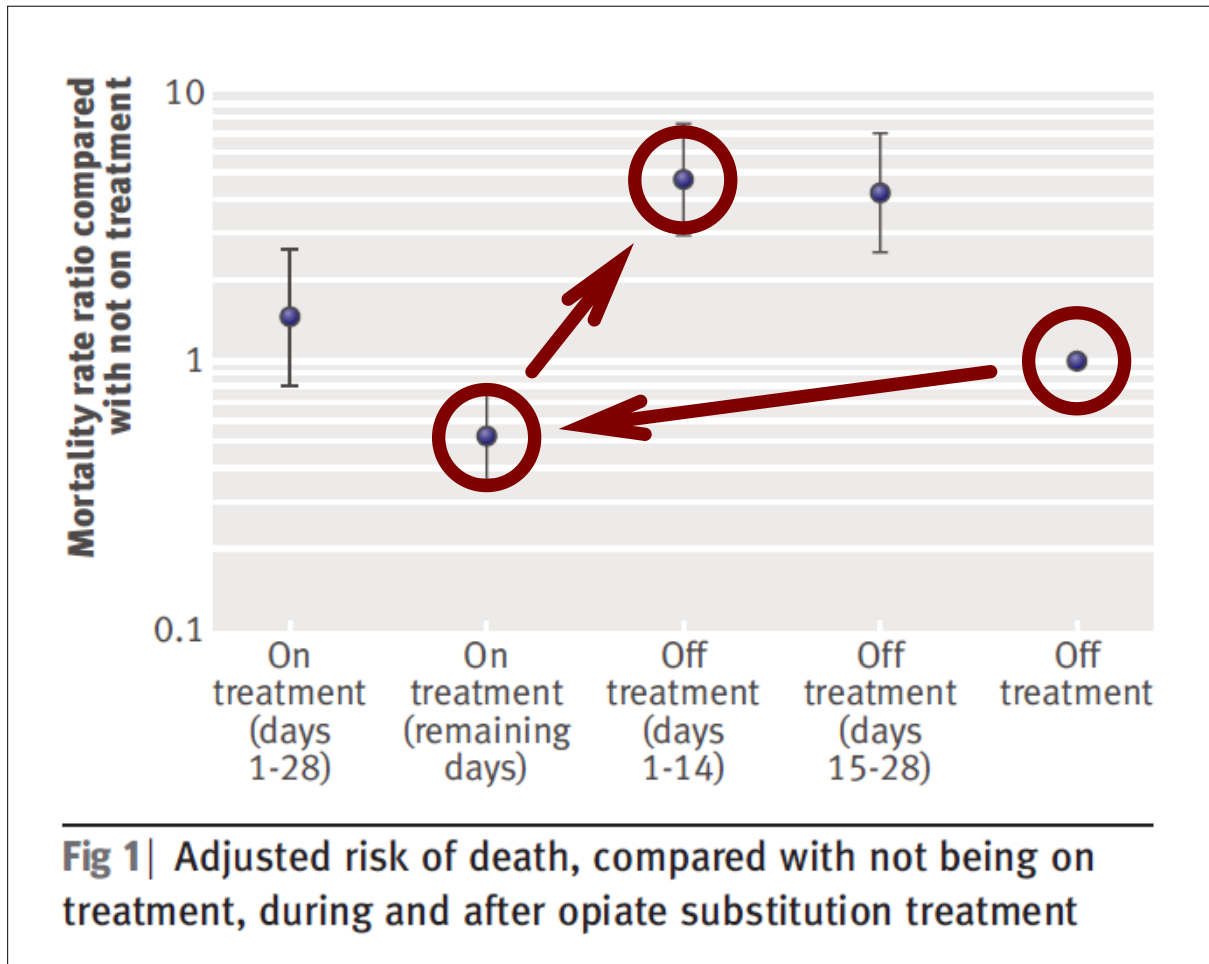
Opiate users have a high risk of death and contribute substantially to adult mortality.¹ Systematic reviews estimate annual death rates of about 1%, which is more than 10 times that of the general population and contributes more than 10% of adult mortality.²⁻⁴ In the United Kingdom and many other countries, most deaths among opiate users are due to overdose, and opiates are the most common cause of poisoning from controlled drugs in the population.^{5,6} Estimates of the prevalence of opiate use in the UK suggest 30-fold increases between 1970 and 2000,⁸ but more recent estimates are stable at around 250 000 opiate users (approximately 0.8% of adults aged 15-64).^{10,11}

Good evidence shows that opiate substitution treatment, primarily with methadone and buprenorphine, is effective across a range of outcomes, including reducing all cause mortality, improving physical and mental health, and decreasing illicit drug use, criminal activity, and risk of HIV infection.¹²⁻¹⁹ In the UK, opiate substitution treatment is delivered mainly within primary care, often through shared care arrangements with specialist drug agencies.^{20,21} In the past decade, opiate prescription has more than doubled while the number of deaths involving methadone and police seizures of methadone have declined, coinciding in part with the introduction and roll-out of greater supervised consumption of opiate substitution treatment.²² However, the overall number of deaths from overdose of opiates has not decreased and targets to reduce deaths from overdose in England and Wales have not been met, despite an apparently stable population taking opiates and considerable investment in treatment.⁴

The risk of death during and after treatment seems to be non-uniform. Treatment guidelines and recent studies have suggested that the start of treatment (the first 28 days) may be associated with an increased risk of death.^{23,24} Furthermore, findings in two large cohorts

UK General Practice Research Database

- 5,577 patients treated for opioid addiction in primary care settings between 1990 and 2005
- Opioid agonist therapy with methadone or buprenorphine
 - 231,000 prescriptions
- Mortality during and after treatment
 - Planned versus unplanned discharges



Pain Management Blunders

Acute Pain Management for Patients Receiving Maintenance Methadone or Buprenorphine Therapy

Daniel P. Alford, MD, MPH; Peggy Compton, RN, PhD; and Jeffrey H. Samet, MD, MA, MPH

More patients with opioid addiction are receiving opioid agonist therapy (OAT) with methadone and buprenorphine. As a result, physicians will more frequently encounter patients receiving OAT who develop acutely painful conditions, requiring effective treatment strategies. Undertreatment of acute pain is suboptimal medical treatment, and patients receiving long-term OAT are at particular risk. This paper acknowledges the complex interplay among addictive disease, OAT, and acute pain management and describes

4 common misconceptions resulting in suboptimal treatment of acute pain. Clinical recommendations for providing analgesia for patients with acute pain who are receiving OAT are presented. Although challenging, acute pain in patients receiving this type of therapy can effectively be managed.

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The treatment of opioid dependence, both on heroin and prescription narcotics, with opioid agonist therapy (OAT) (that is, methadone or buprenorphine) is effective: It decreases opioid and other drug abuse, increases treatment retention, decreases criminal activity, improves individual functioning, and decreases HIV seroconversion (1–5). Because of the increasing use of these medications for prolonged periods in primary care, a practice called *office-based opioid treatment*, nonaddiction specialists will be treating more of these affected patients in clinical practice, including those with episodes of acute pain (6–11).

Adequate treatment of acute painful conditions is an essential dimension of quality medical care (12–17). Inadequate treatment is common among a wide spectrum of patients (18–23). Nonopioid analgesics (for example, nonsteroidal anti-inflammatory drugs and acetaminophen) are recommended for treating acute pain; however, moderate to severe acute pain will often require opioid analgesics (24). Physicians may not prescribe effective opioid analgesia across all patient populations because of fears of cognitive, respiratory, and psychomotor side effects; iatrogenic drug addiction; and prescription drug diversion (25, 26). This tendency of health care professionals to undermedicate patients with opioid analgesics has been termed *opiophobia* (27). Such fears are exaggerated when treating patients with a known history of a substance use disorder. The provision of opioid analgesics to a patient with opioid dependence receiving OAT can be particularly challenging (28, 29).

We highlight the issues associated with the management of acute pain in patients receiving OAT and describe theoretical and empirical findings that suggest unique requirements for opioid analgesia for such patients. In addition, we identify common misconceptions of health care providers that underlie inadequate pain management and provide practical recommendations for the analgesic management of acute pain in this special clinical population. To help illustrate these issues, we present the following clinical vignette from our experience.

A 29-year-old woman reported severe right arm pain after fracturing her olecranon process. She had a history of injection heroin use and received methadone, 90 mg/d, in a methadone maintenance program. In the emergency department, she seemed uncomfortable and received one 2-mg dose of intramuscular morphine sulfate over 6 hours. While hospitalized, she continued to report severe pain despite receiving her daily methadone dose and intramuscular ketorolac. She was told that her usual methadone dose should help control her pain. She was labeled as “drug-seeking” because of her constant requests for additional pain medications.

PAIN AND OPIOID DEPENDENCE

The clinical conditions of pain and opioid dependence are not unrelated phenomena (30–32). Forty-one years ago, Martin and Inglis (33) observed that opioid-addicted patients abuse opioids to treat “an abnormally low tolerance for painful stimuli.” Opioids, whether administered with analgesic or addictive intent, activate opiate receptors in the locus coeruleus and amygdala, which provide both analgesia and reward (34, 35).

The presence of one condition seems to influence the expression of the other. Clinical examples of this include how the presence of acute pain seems to decrease the euphorogenic (pleasurable) qualities of the opioid (36) and how the presence of addictive disease seems to worsen the experience of pain. With respect to the latter, Savage and Schofferman (37) found a decade ago that persons with addiction and pain have a “syndrome of pain facilitation.” Their pain experience is worsened by subtle withdrawal syndromes, intoxication, withdrawal-related sympathetic nervous system arousal, sleep disturbances, and affective

See also:

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Myth #3

- Patients who take buprenorphine don't need pain medications for acute pain

Fact #3

- Maintenance buprenorphine does not offer analgesia
- Conceptualize it like insulin or prednisone
 - Stress of surgery (for example) requires additional coverage

Myth #4

- Prescribing opioids for acute pain risks addiction relapse

Fact #4

- “ There is no evidence that exposure to opioid analgesics in the presence of acute pain increases rates of relapse in such patients
- “ [T]he stress associated with unrelieved pain is more likely to be a trigger for relapse than adequate analgesia ”

Myth #5

- Prescribing opioids to patients who take buprenorphine risks overdose and death

Fact #5

“ The concern about severe drug toxicity with analgesic opioid treatment is not supported by clinical or empirical experience ”

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