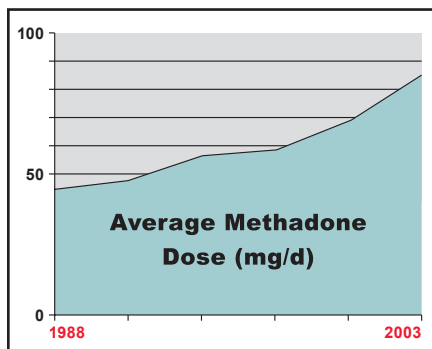


# Forum

THE QUARTERLY NEWSLETTER FOR CLINICAL HEALTH CARE PROFESSIONALS ON ADDICTION TREATMENT

Vol. 12, #2 • SPRING 2003



**The average methadone dose has increased nearly 90% during the past 15 years.**

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## Dose Survey 2003

### Upward Trends Continue

Looking at dosing practices in U.S. methadone maintenance treatment (MMT) programs, incorporating results from a number of surveys spanning the past 15 years,[1-7] there has been an encouraging upward trend toward more adequate methadone prescribing.

For the latest *Addiction Treatment Forum (ATF)* survey, input from readers was solicited during fall 2002 and winter 2003 via a response card and at [www.atforum.com](http://www.atforum.com). This replicated two earlier ATF surveys in 1993 and 1998, with three questions asked about dosing practices at respondents' MMT clinics:

1. *Highest* typical daily methadone dose?
2. *Average* typical daily dose?
3. *Lowest* typical daily dose?

The questionnaire also requested the geographic locale of the clinic, so responses could be divided into regions, and whether the clinic operated on a for-profit or non-profit/public basis.

To better understand dosing practices, the 2003 ATF survey also asked for the percentage of patients receiving methadone doses within each of 5 ranges: < 60 mg/d; 61-80 mg/d; 81-100 mg/d; 101-200 mg/d; >200 mg/d.

### Why Focus on Dose?

There has been long-standing concern within the MMT community regarding the dimensions of an "adequate" or "optimal" methadone dose. In the 1960s, the developers of MMT recommended daily maintenance doses averaging between 80 mg to 120 mg. Further research over the years confirmed that doses exceeding 80 mg/d are more effective than lower doses in terms of retention in treatment and abstinence from illicit opioids.[9,10]

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## Clinical Concepts

### Guidance On Optimal Methadone Dosing

By Peter L. Tenore, MD  
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*Editor's note: During 20 years in the MMT field, Dr. Tenore has cared for more than 5,000 patients on methadone maintenance. He is an advisor to New York OASAS and a frequent lecturer on achieving more adequate methadone dosing. This article is excerpted from a longer paper on the subject that he is developing for future publication.*

Methadone maintenance treatment (MMT), when used correctly, can significantly abolish illicit-opioid use in stabilized patients. A most critical factor is an adequate dose of methadone which should be high enough to block euphoria and sufficient to eliminate opioid withdrawal and craving. *Doses of methadone should be optimized on an individual basis without artificial ceilings, while maintaining caution to avoid adverse effects.*

### Starting Methadone (Induction)

At the start (induction) of MMT, our clinic cautiously and methodically increases daily methadone doses in a protocol-driven manner based on CSAT recommendations, and following careful assessment of the person's prior opioid dependence.[1, see *Table 1*]

The essential advice is to *start low and go slow*. During methadone induction, patients may be in mild withdrawal toward the *end of the dosing interval*, so doses are NOT automatically increased based on how patients feel at 12 or more hours after dosing. Rather, they are asked how they feel at 4 to 10 hours after dos-

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## Events to Note

For additional postings & information, see:  
[www.atforum.com](http://www.atforum.com)

### July 2003

2003 New England School for Treatment of Opioid Dependence  
July 7-11, 2003  
Newport, Rhode Island  
Contact: 207-621-2549; [www.neias.org/](http://www.neias.org/)

### August 2003

American Psychological Association Annual Meeting  
August 7-10, 2003  
Toronto, Canada  
Contact: 800-374-2721; 202-336-5510

### 11th Annual New England Advanced School of Addiction Studies

August 25-28, 2003  
Waterville Valley, New Hampshire  
Contact: 207-621-2549; [www.neias.org/](http://www.neias.org/)

### September 2003

NAADC Conference (National Assoc. of Alcoholism & Drug Abuse Counselors)  
September 14-17, 2003  
Washington, DC  
Contact: 800-548-0497; [naadac.org](http://naadac.org)

### UPCOMING 2003 - 2004...

ASAM State of the Art in Addiction Medicine Conference  
October 30 - November 1, 2003  
Washington, DC  
Contact: 301-656-3920; [www.asam.org](http://www.asam.org)

AMERSA 27th Annual Conference (Association for Medical Education & Research in Substance Abuse)  
November 6-8, 2003  
Baltimore, Maryland  
Contact: [Isabel@amersa.org](mailto:Isabel@amersa.org); 401-349-0000

131st American Public Health Association Annual Convention  
November 16-20, 2003  
San Francisco, California  
Contact: 202-777-2742; [www.apha.org/](http://www.apha.org/)

14th Annual Meeting, American Academy of Addiction Psychiatry  
December 4-7, 2003  
New Orleans, Louisiana  
Contact: 913-262-6161; [www.aaap.org](http://www.aaap.org)

6th International Conference on Pain & Chemical Dependency  
February 5-7, 2004  
New York, NY  
Contact: Lorna Gannon 609-275-5030, [lorna.gannon@Meditech-media.com](mailto:lorna.gannon@Meditech-media.com); [www.painandchemicaldependency.org](http://www.painandchemicaldependency.org)

[To post your announcement in A.T.Forum and/or our Web site, fax the information to: 847-392-3937 or submit it via e-mail from [www.atforum.com](http://www.atforum.com)]

A.T.F.

## Straight Talk... from the Editor

### Momentous Issues at AATOD Drive Forward Momentum in the Field

The AATOD Conference (American Association for the Treatment of Opioid Dependence) continues to be the leading event for the methadone maintenance treatment (MMT) field. The most recent gathering, April 13-16, 2003 in Washington, DC, attracted more than 1000 attendees for an impressive line-up of 10 pre-Conference sessions, 39 workshops, 22 poster presentations, and 35 vendor exhibits put together by Association President Mark Parrino and his organizing committees.

As usual, plenary sessions featured distinguished speakers addressing critical topics. At this Conference, there emerged four particularly momentous issues that will most likely propel the opioid-addiction treatment field forward in months to come.

#### Treatment Vouchers Touted

Anthony A. Williams, Mayor of the District of Columbia, introduced the first momentous issue of the Conference – treatment vouchers. He noted that his city has the first fully functional “Drug Treatment Choice Program” in the country. This approach allows patients themselves to select the treatment they need from among approved providers. Patients are allowed a maximum of \$10,000 to \$25,000 a year in vouchers for treatment services, depending on whether or not they have children, respectively. Their treatment decisions can be based on such factors as convenience or choosing a provider in their own community that better understands their needs.

John P. Walters – Director, Office of National Drug Control Policy (ONDCP), Executive Office of the President – observed that vouchers fund staff and services; not treatment slots as does the current approach, which results in excess capacity in some places and waiting lists in others. He said \$600 million is being committed nationally to voucher programs. In his opinion, this system will increase the number of eligible providers and get services to where they are needed most; although, he conceded it is still unknown how such vouchers will be managed by individual states.

Walters said the ONDCP will be going to the 26 largest cities in the U.S., identifying federal and state treatment

resources and determining how to best use those resources. He asserted that President Bush is a strong supporter of drug treatment and called for help from those assembled at the Conference, since AATOD helps provide a national voice for what is needed and where.

In further support of better patient care, Charles G. Curie – Administrator, Substance Abuse & Mental Health Services Administration (SAMHSA) – said treatment capacity expansion (TCE) grants would be used for targeting specialized needs and his agency has a 5-year “Access to Recovery” plan. For that, SAMHSA has developed a matrix of cross-cutting priority programs and principles based on an underlying philosophy that “people of all ages, with or at risk for mental or substance use disorders, should have the opportunity for a fulfilling life that includes a job, a home, and meaningful relationships with family and friends.”

#### Accountability Matters

The second highly noteworthy issue that emerged was accountability. Congressman Elijah E. Cummings – Representative of the 7th Congressional District of Maryland – affirmed that “Congress wants accountability” and demands will grow for assurances that tax dollars are being spent efficiently and effectively for addiction treatment.

Cummings asserted that there is an ever present need to reaffirm that addiction treatment works. Currie declared in his presentation, “We know treatment works and recovery is real.” And, the ONDCP’s Walters maintained that he does not hear people claiming treatment is ineffective – at least not publicly. Although, he acknowledged, “some people say it works but don’t really believe that it does.”

Drug problems cannot be ignored, Cummings insisted, since drugs are everywhere. He suggested a combination of treatment and police work is needed; yet, he proposed that current laws barring drug offenders from certain types of jobs should be changed. Furthermore, many people with drug problems also have mental problems, he observed, and those mental disorders need to be addressed as a part of recovery.

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## Straight Talk...from the Editor Continued from Page 2

In a rousing speech, bordering on a pep talk, Cummings roared to the audience, "You are appreciated for what you do... treatment works... do not get discouraged. If you touch one person, you help an entire family that extends through generations." He received an enthusiastic standing ovation.

### Drug Deaths of Concern

A third crucial issue was deaths allegedly associated with methadone, and highlighted in several major newspaper articles during the past 6 months. Parrino asserted that most of those fatalities were related to methadone used for pain management, not for MMT. Also, too often, methadone is held responsible even if it is merely present during autopsy and there is no clear medical definition of what might constitute a methadone-caused death.

**Laura Nagel** – Deputy Assistant Administrator, Office of Diversion Control for the Drug Enforcement Administration (DEA) — similarly noted that methadone tablets most often prescribed for pain, rather than the liquid dispensed by most MMT programs, appear to be most problematic. There is a large illicit market for legally manufactured drugs, she said, with 20,000 Americans dying each year of drug-induced causes overall. The cost to the American public for illicit drug trafficking is a staggering \$65 billion each year.

Along those lines, DC mayor Williams said substance abuse costs his city, with a population of only 600,000 persons, \$1.2 billion per year. Furthermore, 20% of substance-abusing persons in DC are ages 12 to 18.

### Buprenorphine Discussed

The fourth significant focus at the Conference was on buprenorphine, now approved for addiction therapy. Parrino said AATOD is hopeful that buprenorphine will expand access to treatment for those who need it and eventually be used within MMT programs. However, he stressed that treatment *services*, in addition to medications, are still critical for attending to individual patient needs and these should not be lost in the interest of merely medicating more patients. This message was reinforced by the DEA's Nagel, who said that her agency supports greater access to treatment, but such treatment should go beyond just providing a drug.

Four workshops at the Conference were devoted to buprenorphine and several others discussed it. However, MMT clin-

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icians and administrators we spoke with were hesitant about adding the opioid agonist to their treatment offerings in the future.

### Accreditation Falling Behind

To recap, there were four significant and vital issues coming from this year's AATOD Conference that will certainly drive the field forward during coming months: 1) innovative programs for providing greater access to treatment (such as, vouchers); 2) treatment providers assuming greater responsibility for outcome success (accountability); 3) curtailing drug-related deaths (some involving methadone, but also encompassing all opioid agents); and, 4) newly approved buprenorphine that might help expand treatment enrollment.

Underlying all of those issues, the MMT program accreditation process is continuing. However, in opening the Conference, Parrino noted that 40% of MMT programs still needed to be surveyed for accreditation and, for unknown reasons, many had not applied for an extension of the May 2003 deadline. This was of great concern, and could result in fewer MMT programs in the U.S. The Center for Substance Abuse Treatment (CSAT) was sending letters to those programs, notifying them of the availability of a deadline extension, and will be studying the impact of the accreditation process in improving patient care.

As usual, "interesting times" lay ahead. We're already looking forward to learning how the issues progressed at the next AATOD Conference, which will be in fall 2004 in Orlando, Florida – a wonderful

spot for combining some fun with business. Mark your calendar now.

### Respond to Reader Surveys

#### "Graying of Methadone"

The feature on "The Further 'Graying of Methadone'" in our last edition (Winter 2003) gathered much attention. Yet, there were few responses to the e-survey at our web site to gather more information.

To understand the full extent of this situation, we need data on how many patients in MMT fall into the "graying" category around the country. *Please help by responding to the following questions:*

1. What percentage of your MMT patients fall into the following brackets:  
\_\_\_% under age 21; \_\_\_% 21-29;  
\_\_\_% 30-39; \_\_\_% 40-49; \_\_\_% 50-59;  
\_\_\_% 60 and above.
2. What is your total number of MMT patients? \_\_\_\_\_.
3. How long has your MMT program been in operation? \_\_\_ years.
4. Please indicate city & state in which you are located: \_\_\_\_\_

#### Internet Access?

As you may know, all *AT Forum* contents are available free at our website – **www.atforum.com**. We are interested in learning how many readers have access to the Internet and make use of our website. Please take a minute and respond to our Internet Access Survey.

*There are several ways to respond to AT Forum surveys:* **A.** provide your answers on the postage-free feedback cards in this issue; **B.** write, fax, or e-mail [info below]; or, **C.** visit our web site to respond online. As always, your written comments also are important for helping us discuss the results.

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# EBAM\* Booklets Available on Web

(\*Evidence-Based Addiction Medicine)

There is an urgent need in the addiction treatment field for *good science* to help overcome stigma, prejudice, and misunderstanding. Yet, all medical research is imperfect, and being able to distinguish good from bad research is critical for adopting valid practices to improve patient care and outcomes.

ADDICTION TREATMENT

## Forum

EBAM\* For Practitioners

(\*Evidence-Based Addiction Medicine)  
Evaluating & Using Research Evidence in Clinical Practice

Stewart B. Leavitt, PhD  
Sponsored by an educational grant from Mallinckrodt, Inc.

**New Outlooks on Addiction Research**

Medical research is an imperfect science. Research in substance dependency (addiction) is no exception and, in fact, has its own limitations. Understanding those imperfections is essential for becoming a more critical reader of addiction research literature and a more discerning consumer of scientific evidence.

Just as jurors need evidence from reliable witnesses or forensic investigators to arrive at impartial and fair verdicts, addiction treatment providers need credible information to answer health-care questions and make clinical decisions. Yet, the amount of information in the addiction field has rapidly increased, bringing with it challenges of navigating efficiently through the mushrooming number of articles and identifying evidence that is of valid and reliable quality.[1]

Toward those ends, the booklet describes some fundamental principles for evaluating and using research evidence in clinical practice. It provides knowledge to determine if a research article is relevant to clinical information needs, and if the results are likely to be valid for a particular purpose.

Many of the concepts may be unfamiliar to readers and will require careful study. This booklet is best designed slowly and then used as a reference when evaluating research in addiction medicine.

Contents		
New Outlooks	Cohort Studies	Importance of Power
Caveat Lector	RCTs	Bottom-line Clinical Effects
The Role of EBAM	Reviews & Meta-analyses	Estimates of Effect
Problems of Proof	Assessing Validity of Research	Confidence Intervals
Reasoning with Research	Delimiting Bias	Forecasting
Addiction Research Approaches	Publication Bias	Survival Analysis
Hypothesis Testing	Patient Selection	Correlation
The Null Hypothesis	Confounding Factors	Why Good Research Goes Bad
Statistical Significance	Randomization	Design, Execution, Reporting
Clinical Significance	Blinding (Masking)	Post Hoc Analysis
Types of Studies	Placebo Effects	Fallacies of Reasoning
Levels of Scientific Evidence	Recall Bias	Mass Media Distortions
Persuasive Articles	Compliance & Followup	Putting Research into Practice
Case Reports	ITT vs Per-Protocol	Everyday Relevance
Case-Control Studies	Clinical Relevance of Statistics	Healthy Skepticism
		References

Principles of evidence-based addiction medicine (EBAM) provide the necessary tools for understanding and critically assessing research articles and reports, including often-puzzling statistical data, and putting best practices to work. Several free learning aids by *AT Forum* editor Stewart B. Leavitt, PhD – from his workshop at the recent AATOD 2003 Conference in Washington, DC – are available:

- **“Can Addiction Research Be Trusted?” – 6-page introductory booklet, PDF file.**
- **“EBAM\* for Practitioners (\*Evidence-Based Addiction Medicine)” – a more advanced and comprehensive 16-page manual, PDF file.**
- **Companion PowerPoint slides from the AATOD workshop.**

All 3 items may be downloaded *free* at <http://www.atforum.com> (look under the “Addiction Resources” tab).

## Dose Survey 2003 Continued from Page 1

Newer research suggests that some patients require individualized doses exceeding 200 mg/d.[10]

However, during the 1970s, regulatory constraints, stigmatization, and treatment philosophies without a scientific basis resulted in many patients being undermedicated. Quite low average doses became the norm and 100 mg/d was considered the ultimate dose with few exceptions – sort of a “glass ceiling.”

These practices prevailed and methadone maintenance doses averaged merely 45 mg/d in a 1988 survey, with a typical highest dose of 79 mg/d.[1] Largely due to inadequate dosing practices, in 1990, the U.S. General Accounting Office (GAO) reported to Congress that the MMT system had fallen into disarray and programs were not effective in achieving the benefits of methadone maintenance.

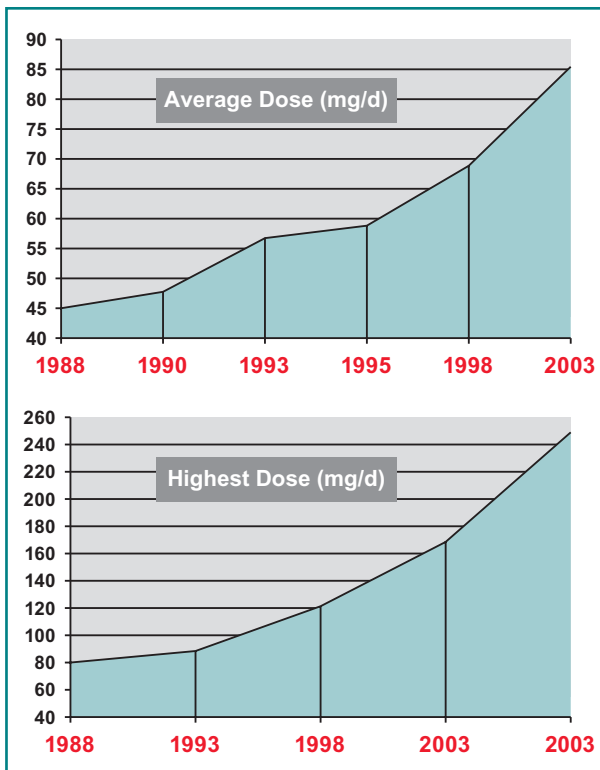
The GAO report may have served as a “wake-up call,” for soon thereafter an upward trend in methadone dosing practices became evident. The purpose of the current ATF survey was to update earlier studies and plot the trend over 15-years.

### Noteworthy Results

Numbers of responses to ATF methadone dose surveys have remained high – 269 (2003); 251 (1998); 203 (1993) – with most, but not all, respondents answering every question. Some noteworthy trends have emerged, as reflected in the *graphs* and in the *Table 1* data, which provides greater statistical detail.

**Average Dose** – During the 15-year span, there was a consistent and statistically significant upward trend in average daily methadone doses, reaching 85.2 mg/d in 2003; nearly a 90% increase from 1988. However, 16% of respondents indicated average doses were still less than 60 mg/d.

**Highest Dose** – Similarly, there was a significantly large rise in highest doses, reaching 169.4 mg/d in the 2003 ATF survey, or more than a 2-fold increase from the 79 mg/d reported in 1988. In May 2003, AATOD (American Association for the Treatment of Opioid Dependence) made available data from an informal sur-



vey of its members that produced a much larger number (248.6 mg/d), representing more than a 3-fold increase over 1988.

This discrepancy might have resulted from AATOD asking for the “largest dose prescribed”; whereas, the ATF survey requested the “highest typical” dose. The AATOD survey included 38 MMT programs in 34 states, encompassing about 31,000 patients. Traditionally, doses reported in this “highest” category have varied over broad ranges, suggesting in some cases that one clinic’s largest dose is another program’s average dose.

**Lowest Dose** (not charted) – This question has been confusing to readers and responses are confounded by the inclusion of patients being tapered off of methadone, so the “typical” lowest dose is difficult to define. This number has remained fairly steady throughout ATF surveys – 21.8 mg/d (1993); 27.6 (1998); 27.5 (2003) – although its significance cannot be determined.

Since averages can be deceiving, the 2003 ATF survey asked the dosing-range questions to better gauge specific proportions of patients above and below certain dose levels. Results are depicted in the *bar graph*.

In this analysis, a significant percentage of patients (22.5%) were still receiving doses less than 60 mg/d; although, as with the “lowest dose” question, it is not known what portion was on declining doses as part of a medically supervised

## Dose Survey 2003 Continued from Page 4

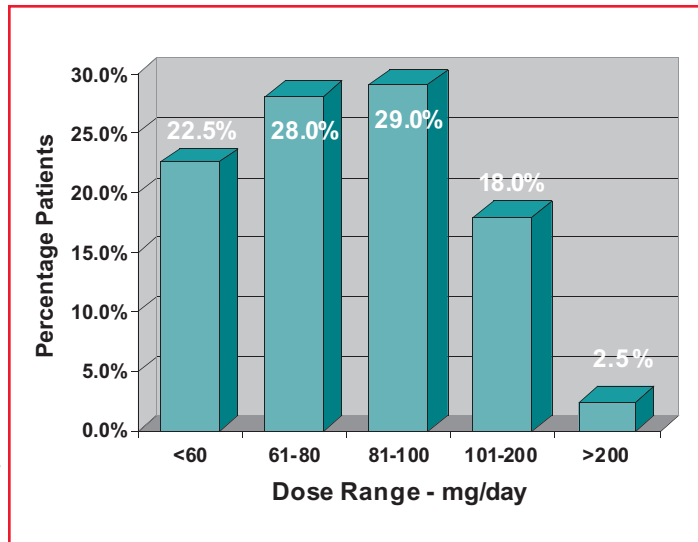
withdrawal regimen. Still, this trend is improving, since other researchers found that the percentage receiving less than 60 mg/d was 35.5% in year 2000, and this was vastly improved from the nearly 80% administered such low doses in 1988.[9]

Those same researchers noted that only one-third of patients in 2000 were receiving doses greater than 80 mg/d.[9] Whereas, the ATF survey found this had increased to nearly half of patients by 2003.

Most of the research to date has not sufficiently explored upper-range dosing above 100 mg/d, but those studies that have done so reported relatively large proportions of patients requiring doses greater than that level to achieve the most favorable treatment outcomes.[10] The ATF 2003 survey found that only one-fifth of patients (20.5%) received doses greater than 100 mg/d, which suggests the persistence of a “glass ceiling” whereby such higher doses are considered an exception in most MMT programs.

### Encouraging Trends

The nearly 90% increase in “average dose” during the past 15 years is encouraging. Yet, the fact that only about half of



patients receive 80 mg/d or more suggests there is much room for improvement.

While some patients can do well on lower doses of methadone, and “more” may not *always* be better, available research evidence indicates that as doses increase to more optimal individualized levels treatment outcomes improve.[9] And, there are early indications of a relationship between MMT clinic accreditation and more adequate dosing practices,[10] so the upward trends are likely to continue for some time.

Coming up in the next issue of *AT Forum*: a look at results on a regional basis and comparisons of for-profit vs. non-profit/public clinic operations, including results from outside the U.S.

1. D'Aunno T, Vaughn TE. Variations in methadone treatment practices: Results from a national study. *JAMA*. 1992;267(2): 253-258.
2. D'Aunno T, Folz-Murphy N, Lin X. Changes in methadone treatment practices: results from a panel study, 1988-1995. *Am J Drug Alcohol Abuse*. 1999; 25(4):681-699.
3. United States General Accounting Office. Methadone maintenance: some treatment programs are not effective; greater federal oversight needed. 1990 (March). Report No. GAO/HRD-90-104. [Non-random survey of 24 programs in 8 states.]
4. ATF dosage survey: The results are in. *Addiction Treatment Forum*. 1993; 2(3):1.
5. Dosage survey '98: Changes for the better. *Addiction Treatment Forum*. 1998;7(3):1.
6. *AT Forum* dosage survey conducted during fall-winter, 2002-2003, and reported here.
7. AATOD (American Association for the Treatment of Opioid Dependence) survey during spring 2003. Data provided by Mark Parrino, May 8, 2003.
9. D'Aunno T, Pollack HA. Changes in methadone treatment practices: results from a national panel study, 1988-2000. *JAMA*. 2002;288(7):850-856.
10. The methadone dose debate continues. *Addiction Treatment Forum*. 2003;12(1):1. Available at: <http://www.atforum.com>.

A.T.F.

## Looking Closer at the Data

### Table Notations

MEAN = average score (mg/d); N = Number of respondents/programs; SD = Standard Deviation (mg/d); NR = Data Not Reported; \* = significant differences between these data points across the respective row;  $p < 0.01$  (via simple t-tests). References for studies corresponding to each date are at the end of the article.

### Survey Limitations

ATF surveys are useful for sensing the direction and scope of trends, but they are not promoted as being scientifically rigorous, and the ATF sampling cannot be considered truly random. All readers are invited to respond and a self-selection bias is probable. However, from available information, it appears that nearly all respondents were clinic staff with access to accurate data.

Interpretation of the terms “typical,” “highest,” “average,” and “lowest” was open-ended and may have been unclear to some

respondents. Some surveyors – e.g., those by D'Aunno and colleagues[1,2,9] – have overcome this difficulty via telephone interviews with respondents to verify data.

Data collected via ATF surveys are not censored to delete extreme scores that might be considered “outliers,” which sometimes results in higher sample variance, although it seems reasonable to speculate that there were consistent sampling and response errors across the 1993, 1998, and 2003 surveys. The consistently upward trend reflected in ATF data, and its concordance with trends reflected in all of the other surveys, suggests that the overall results are most probably valid and reliable.

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**TABLE 1: Methadone Dosing - 15 Year Trend Data**

	1988 <sup>1</sup> MEAN N; SD	1989 <sup>2</sup> MEAN N; SD	1990 <sup>3</sup> MEAN N; SD	1993 <sup>4</sup> MEAN N; SD	1995 <sup>2</sup> MEAN N; SD	1998 <sup>5</sup> MEAN N; SD	2003 <sup>6</sup> MEAN N; SD	2003 <sup>7</sup> MEAN N; SD
<b>Highest Dose</b> mg/d	79.0* 172; 20.0	NR	NR	89.1* 201; 19.6	NR	123.0* 247; 92.4	169.4* 268; 120.4	248.6* 38; 102.2
<b>Average Dose</b> mg/d	45.0* 172; 10.0	46.0 140; NR	48.0 24; NR	56.6* 196; 3.0	59.0 116; NR	69.4* 237; 26.2	85.2* 263; 45.1	NR

<b>Table 1: Start-up Protocol</b>	
<b>DAY</b>	<b>METHADONE DOSE</b>
1	30 mg
2	40 mg
3	50 mg/d (maintain for 5 days – range 4-10 days – to reach steady-state)
7 to 13	60 mg/d (maintain dose for 5 days)
12 to 18	70 mg/d
Every 5 days (range 4-10)	+10 mg/d (as needed)

ing, and if they feel well no increase is given the following day. If patients experience sedation, we reduce the dose, maintain that an additional 5 to 7 days for more opioid tolerance to develop, and then resume the increase if it seems appropriate. If the patient is still experiencing opioid withdrawal symptoms at 70 mg/d, which can take 12 to 18 total days to achieve, we continue to increase the dose by 10 mg/d every 5 days until there are no withdrawal symptoms and then hold the dose at that level. It takes about 5 days (range 4-10 days) to reach a steady state at each new dose level, and more rapid dose increases may result in a harmful accumulation of methadone.

Once the patient is on a steady dose that eliminates opioid withdrawal, the dose is maintained for 4 weeks while urine toxicology screens are monitored. Illicit opioids are often detected in week 1 and 2 as patients “test” the opioid blockade of methadone, so we usually do not increase doses based on those results. If no opioid abuse is detected during week 3 and 4, the methadone dose is maintained. If opioid blockade has *NOT* been fully established, opioid abuse usually continues – evidenced by opioid-positive toxicology at week 3 and/or 4 – and the methadone dose is increased by 10 mg/d followed by 4 more weeks of monitoring.

This process of 10 mg/d increases and 4-week monitoring continues until the toxicology studies from week 3 and 4 are negative for opioid abuse. Waiting several weeks between dose increases ensures that there will

be little if any sedation or other signs/symptoms of methadone over-medication.

Higher doses of methadone are often necessary and have been demonstrated as safe, if increments are kept to 10 mg/d or less and sufficient time elapses between dose increases. In our clinic, doses of 110 to 150 mg/d are commonly required, but some patients need doses well-above 200 mg/d, often guided by serum methadone level monitoring.

However, it is important to note that patients with debilitating illness or who are sensitive to opioid effects may require lower doses and longer intervals between dose increases.

### Introducing DINO-VAMP

To help guide methadone dose increases, we developed an acronym – DINO-VAMP – as a reminder to consider all issues for optimizing dosing. Each letter represents an important element (see *Table 2*).

“D” is a prompt to inquire about continued Drug abuse, including heroin or other opioids. Are patients experiencing euphoria (i.e., not “blocked” by methadone)?

This also is a reminder to review the patient’s Dose of methadone. The amount must be sufficiently high to block euphoria and prevent opioid withdrawal without causing sedation.

“I” prompts to ask about Interactions between methadone and other drugs. Since methadone is primarily metabolized in the liver by CYP450 enzymes, drugs that alter this system by inducing or inhibiting

enzymes can significantly lower or elevate methadone serum levels, respectively.[2]

We have found that patients experiencing opioid withdrawal due to a drug interaction usually require methadone increases. However, each case must be individualized, and daily or every other day observation during this period is advisable to avoid methadone over-medication.

“N” refers to Neuroleptic medications as a reminder to consider psychiatric disorders in patients requiring methadone increases. Nearly half of patients enrolling in MMT have psychiatric disorders and often need higher methadone doses for stabilization.[3]

“O” is a reminder to inquire about Opioid withdrawal (abstinence) syndrome. Patients ultimately should be “comfortable” 24 hours each day, without having to suffer subjective symptoms or objective signs of withdrawal. In our experience, most patients do not have objective signs, only subjective complaints (e.g., “I’m not comfortable” or “My dose isn’t holding me”). These cases should be considered for a methadone increase, or patients will begin to self-treat withdrawal with illicit opioids.

“V” represents Vitamin C. This agent, as well as all other urinary acidifiers (e.g., K-Phos, citrus fruit juices), in high quantities can act as a “pH trap” for methadone, removing it from circulation by increasing renal excretion.[4] If withdrawal occurs, patients should lower intake of vitamin C or the other substances. When urine acidification is needed for urologic reasons, methadone dose increases may be needed.

The “V” also is for Virus. Some research suggests that patients with HCV may require much higher methadone doses[5]; although, one study indicated this may not be necessary.[6] During HCV infection, and its treatment with antiviral agents, methadone dose adequacy should be closely monitored.

“A” is for Atmosphere, which addresses stress in the patient’s environment. Stressful life events may prompt a relapse or increase opioid abuse, so we need to help identify and rectify the difficulties, and respond appropriately to patients’ requests for dose increases during such times.

“M” is a prompt to consider Menopause as potentially causative of an opioid withdrawal-like

<b>Table 2: DINO-VAMP – Factors Influencing Methadone Dose Adjustment</b>	
<b>D</b>	Drug abuse (may indicate inadequate methadone dose) Dose (adequacy must be monitored)
<b>I</b>	Interactions (with other medications or herbal products may affect methadone potency)
<b>N</b>	Neuroleptics (Patients with psychiatric illness may require methadone dose adjustments)
<b>O</b>	Opioid withdrawal signs/symptoms
<b>V</b>	Vitamin C (Urinary acidifiers can cause more rapid elimination of methadone) Virus (HCV sometimes, but not always, incurs a need for higher methadone doses)
<b>A</b>	Atmosphere (Stress at home, work, etc. may foster a request for higher dose)
<b>M</b>	Menopause (symptoms may mimic opioid withdrawal) Medical conditions (may require special management)
<b>P</b>	Pregnancy (affects methadone dosing requirements) Plasma – i.e., serum – levels (may need monitoring)

Continued on Page 7

syndrome. Many menopausal symptoms overlap those of opioid withdrawal, causing some women to ask for increased methadone. Differentiating menopause from opioid withdrawal requires attention to patient history and, possibly, laboratory tests. In our experience, blood levels of estradiol under 30 ng/mL and methadone trough serum levels above 300 ng/mL support menopause, rather than opioid withdrawal due to insufficient methadone.

“M” also reminds us that most Medical conditions, especially cardiovascular illness, will be more difficult to manage if patients are in even minimal opioid withdrawal. Withdrawal – with its elevations in pulse, blood pressure, and catecholamines – can make the management of angina, hypertension, and diabetes more difficult.

“P” refers to Pregnancy, which may be associated with decreased absorption of methadone, plus volume expansion and increased metabolism, that lowers blood methadone levels.[7] Pregnant women may develop opioid withdrawal (especially during the third trimester) and request an increase in methadone dose.[8] Because opioid withdrawal can lead to maternal-fetal complications – including eclampsia, prematurity, and spontaneous abortion – doses may be increased by 10 to 20 mg once or twice a week or more often, with possible split dosing, if withdrawal signs/symptoms develop.

The “P” also stands for methadone Plasma level (although, measurements are actually made in blood *serum*, which is plasma devoid of fibrinogen and other clotting factors). Basically, abnormally low serum levels often result in withdrawal distress and subsequent opioid abuse. Demonstrating to patients just how low their levels are is often helpful in convincing them of the need for higher methadone dose.

**Using SMLs Effectively**

Serum methadone levels (SMLs) can be helpful in arriving at the most adequate dose, in justifying higher doses, and in identifying patients who may benefit from split daily dosing. We consider evaluating trough (low point prior to the next dose) and peak (2-4 hours post-dosing) serum levels when patients appear to need increases beyond 150 mg/d of methadone and at every 30 to 40 mg/d increase thereafter.

We seek to achieve a trough level of 400 to 500 ng/mL and a peak level of no more than twice that amount (e.g., 800-1000 ng/mL). Lower or much higher levels

might be acceptable if patients are illicit-opioid-free and exhibit neither withdrawal nor sedation (over-medication). The clinical presentation of the patient should always override the serum level values.

In our clinic, we divide trough serum methadone levels into several ranges for interpretation (*Table 3*). Trough levels of 200 ng/mL or less are considered subtherapeutic, while 400 ng/mL or more is typically associated with less illicit-opioid use and lower opioid withdrawal symptom scores.[1]

To justify high-dose methadone (e.g., greater than 200 mg/d) it can be important to demonstrate that trough serum levels are relatively low in those patients. In our experience, trough levels below 300 ng/mL provide independent validation of a patient’s complaint of withdrawal. Trough levels greater than 500 ng/mL should prompt close clinical monitoring, the overriding concern being over-medication (i.e., sedation and/or respiratory depression). If trough level is above 700 ng/mL, we usually discount withdrawal and look for other reasons the patient might be uncomfortable (e.g., psychiatric or medical disease) and methadone increases are not usually given.

There are rare patients who require very high trough serum levels (such as, 800 ng/mL or much more) and hundreds of milligrams of methadone per day. These doses can be well-tolerated, provided dose escalation is gradual and the patient is cautiously monitored for signs/symptoms of over-medication.

**Split Dosing Helpful For Some**

At any dose, if the peak serum level is more than twice the trough level (P:T > 2.0) – with the patient feeling sedated about 3 hours after dosing but experiencing withdrawal before the next dose – splitting the daily methadone dose should be considered. If the peak-to-trough ratio is greater than 2.0, further dose increases will only further elevate the peak level, not the trough level, resulting in greater sedation during the day but continued opioid withdrawal later on. Splitting the dose may eliminate this problem.

Split dosing begins by administering the usual dose (e.g., 160 mg) on the morning of day 1 and dispensing half (e.g., 80 mg) for 12 hours later the same day. On day 2, the half dose (e.g., 80 mg) is continued twice daily (Q12h). If needed, 5 to 10 mg

**Table 3: Interpreting Methadone SML Values**

TROUGH LEVEL	CLINICAL EFFECT
≤ 200 ng/mL	Subtherapeutic, withdrawal likely.
> 200 - 400 ng/mL	Sometimes little or no withdrawal, but opioid blockade probably incomplete.
> 400 - 500 ng/mL	Optimal: usually no withdrawal, opioid blockade achieved.
> 500 - 700 ng/mL	Withdrawal unlikely, but possible: monitor clinically for over-medication.
> 700 ng/mL	Withdrawal unlikely, look for other reasons for any discomfort (monitor for over-med.).
Patient’s clinical presentation should override SML values.	

methadone can be added to each dose (e.g., 90 mg Q12h, then 100 mg Q12h, etc.) allowing a week between increases. Some patients will need increases more often but they should be carefully monitored for sedation, and weekly trough blood levels might be monitored.

1. Payte J, Khouri E. Chapter 5: Principles of methadone dose determination. In: Parrino MW. State Methadone Treatment Guidelines. Treatment Improvement Protocol (TIP) Series 1. Rockville, MD: U.S. Department of Health and Human Services, Center for Substance Abuse Treatment; 1993. DHHS Pub# (SMA) 93-1991.
2. Gourevitch MN, Friedland GH. Interactions between methadone and medications used to treat HIV. Mt Sinai J Med. 2000;67(5-6):429-443.
3. Maremanni I, Orietta Z, Aglietti M, et al. Methadone dose and retention during treatment of heroin addicts with Axis 1 psychiatric comorbidity. J Addict Dis. 2000;19(2).
4. Nilson et al. Effect of urinary pH on the disposition of methadone in man. Eur J Clin Pharm. 1982;22:337.
5. Leavitt SB. HCV paradoxically increases methadone dose requirement. Addiction Treatment Forum. 2000;9(4). Available at <http://www.atforum.com>.
6. Litwin AH, Gourevitch MN. Does hepatitis C (HCV) virus infection alter methadone dose requirements? Presented at: 129th Annual Meeting of American Public Health Association; October 23, 2001; Atlanta, GA. Abstract #26390.
7. Jarvis MAE, Wu-Pong S, Kniseley JS, Schnoll SH. Alterations in methadone metabolism during late pregnancy. J Addict Dis. 1999;18(4):51-60.
8. Pond S, Kreek M, Tong T, Raghuanath J, Benowitz N. Altered methadone pharmacokinetics in methadone maintained pregnant women. J Pharmacol Exp Ther. 1985;233:1-6.

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## Language Makes A Difference

Remarkable progress has been made in understanding and treating drug-dependence (addiction) as a medical disease. Consequently, addiction medicine has come a long way in achieving parity with other medical specialties. Yet, there is still a prevalence of inappropriate slang that plagues verbal and written communications in the field.

Language does make a difference, and this goes beyond mere "political correctness" to ultimately affect patient care. *AT Forum* has previously championed the cause of avoiding slang in favor of medically appropriate terms in everyday communications (Summer 2001; Vol. 10, #3). More recently, during the ASAM 2002 Review Course last fall, Edwin A. Salsitz, MD and Shannon C. Miller, MD also rallied against the use of "street slang." This was followed by a perspectives article in *ASAM News* (November/December 2002; Vol. 17, No. 6).

The *table* is adapted and expanded from that ASAM article. Common slang terms are paired with more appropriate medical terms, although readers should be able to add even more to the list.

As Salsitz and Shannon acknowledge, "communication in a clinical setting is of paramount importance, and the use of slang terms occasionally may be necessary for clarity with patients." However, in other areas of medicine, patients do learn proper medical terminology from their healthcare providers. "Why shouldn't our medical discipline try to instill a medical vocabulary to describe what we all know is a chronic medical disease?" they write.

The continued use of slang in the addiction treatment field will only further stigmatize professionals and patients alike, create more prejudice, and lead to less rather than greater understanding. Additionally, as noted in a prior *AT Forum* survey (Winter 2002; Vol. 11, #1), nearly 100% of respondents agreed that language affects attitudes and about 80% felt that the use of appropriate medical language helps foster successful recovery.

As a final note, another *AT Forum* survey (Winter 2001; Vol. 10, #1) found that a vast majority of healthcare professionals

SLANG	MEDICAL TERM
addict, junkie, dope fiend, crack head, pot head, hard-core addict, etc.	opioid-addicted patient, cocaine-addicted patient, etc.
smack, blow, angel dust, grass, etc.	heroin, cocaine, phencyclidine (PCP), marijuana (learn and use clinically accurate names)
clean urine	urine negative for drug x, y, z; negative drug toxicology screen
dirty urine	urine positive for drug x, y, z
drunk, smashed, bombed	intoxicated
speed-balling	using heroin/cocaine combination
meth	methadone or methamphetamine (be specific)
strung out	debilitated, intoxicated
cop	obtain, purchase
fix	dose
fixings, fit	drug-using equipment
hooked	drug-dependent, addicted
kicking	detoxifying from drug x, y, z
detox	medically supervised withdrawal (MSW)
Add your own examples....	

and patients preferred use of the term "patient" rather than "client" for persons in addiction treatment. In contrast, non-medical staff were ambivalent about which to use, with most using "client," and many government agencies still appear to vacillate between the two terms. Perhaps, it is time for practitioners, staff, and agencies involved with managing the disease of addiction in healthcare settings to adopt "patient" in all verbal and written communications. As one reader commented, "Using the term client 'demedicalizes' the treatment process."

A.T.F.

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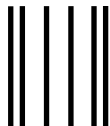
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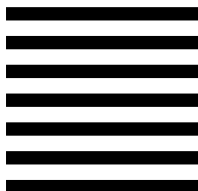
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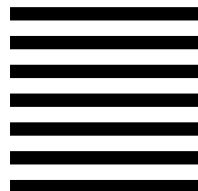
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