

# *Retrospective Review and Practical Analysis of Implementing a Methadone Nomogram to Convert Patients from Morphine Equivalent to Methadone*



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## *Outline*



★ Pain control - overview



★ Brief background of the study



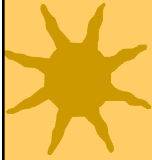
★ Presentation of study

★ Conclusion / discussion

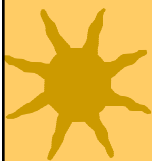
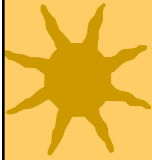
★ Questions



## Overview



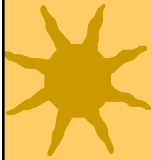
- \* Pain is a ubiquitous aspect of human experience and epitomizes human suffering.
- \* Historically, we have done a poor job of addressing pain.
- \* All of us experience pain in life. People look to clinicians for relief from pain when it becomes difficult to bear.
- \* Our duty to alleviate the suffering brought upon by pain dates back to the very roots of what it means to be a healer.



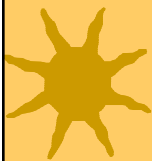
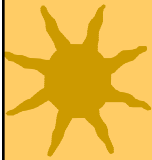
Good, M. et al., eds. Pain as Human Experience. 1992, University of California Press: Berkeley, p. 1



## Pain



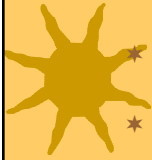
- \* Pain is the most common presenting complaint to physicians in the United states
- \* It has been estimated that 85% to 95% of pain syndromes, can be adequately palliated using relatively simple techniques or medications
- \* A study of the treatment of nonmalignant pain in 49,971 nursing home patients found that 25% of patients with daily pain received no analgesics whatsoever.\*
- \* Advanced age (>85), male sex, cognitive impairment, and being a member of a racial minority were statistically significant risk factors for receiving no analgesics.



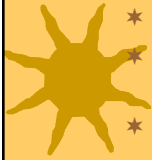
\*Won, A. et al. Correlates and management of nonmalignant pain in the nursing home. SAGE Study Group. Systematic assessment of geriatric drug use via epidemiology. J Am Geriatr Soc 1999; 47(8): 936-42.



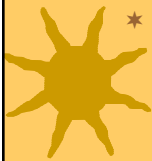
## *Chronic Pain*



- \* Chronic pain is very different from acute pain. It serves no biological purpose.
- \* Chronic Pain is subjectively experienced and objectively displayed in a very different way.



- \* Chronic pain is characterized by physical and mental withdrawal.
- \* Signs very similar to those found in depression, such as anorexia, anhedonia, lethargy, and sleep disturbance are often present.
- \* Chronic pain frequently coexists with depression, making it difficult at times to distinguish between the two.

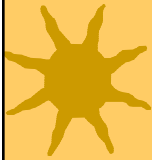


- \* Lack of recognition of chronic pain and difficulty empathizing with it are major barriers to successful treatment

*James L. Hallenbeck, Palliative Care Perspectives, Copyright © 2003 by Oxford University Press, Inc.*

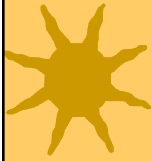


## *Background of Study: Methadone*



- \* Methadone has a long half-life, which allows it to be used on a BID or TID schedule for most patients.

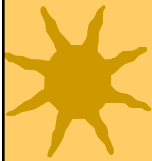
- \* Methadone is cheap.



- \* It has relatively long half-life and large volume of distr.

- \* Blocks n-methyl-D-aspartate (NMDA) receptors, which may be helpful in refractory pain syndromes.

- \* Considerable controversy has arisen regarding conversion ratios for methadone.



- \* Experts have noted a useful principle: the higher the dosage of the opioid being converted to methadone, the lower the conversion methadone dose should be.



## *Methadone*

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★ Traditional conversion ratios

★ Proper conversion is dependent upon a variety of factors –



- drug dosage,
- cross-tolerance among opioids,
- drug interactions,
- physiologic differences in drug metabolism,
- polymorphic variability.



- The conversion process must take into account such factors as the amount of residual drug in the patient's system.
- The time to achieve steady-state blood levels with the new drug, as well as individual patient responses during the conversion process.



## *Study objective*

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★ The objective of this study is to attempt to establish a valid and user-friendly nomogram of which clinicians can rely upon to convert patients on chronic opioid therapy to methadone.



★ This formula was tested retrospectively to validate the formula.



★ Prospective study would be initiated.

# Ripamonte conversion

## Methadone Conversion Study

- Ripamonti, et al 1998
  - Cross-sectional
  - Morphine to methadone
  - 38 patients

### Dose Ranges

Morphine (mg)

30-90

91-300

301 and higher

Morphine to Methadone Ratio

3.70 to 1

7.75 to 1

12.25 to 1

J Clin Oncol 1998;16:3216-3221



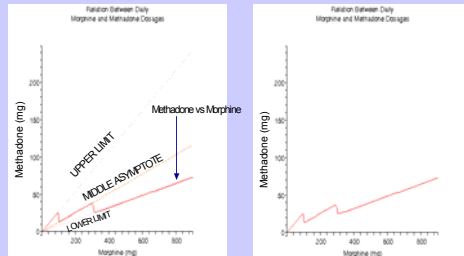
## Fudin Factor

**"Fudin Factor"**  
A Methadone Conversion Formula

$$\text{Methadone (mg)} = \frac{X}{21} \left\{ 5.7 - 3 \sin \left( \frac{90}{\left( \frac{100}{X} + 1 \right)} \right) - \sin \left( \frac{90}{\left( \frac{310}{X} + 1 \right)} \right) \right\}$$

Let X= Morphine (mg)

Most exact to data from Ripamonti, et al 1998, less flowing and unlikely in real life



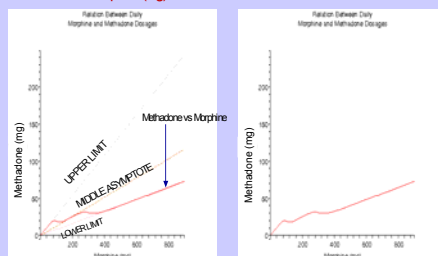
Formula derived by Jason Fudin (Engineering Student, McGill University) in collaboration with Dr. Jeffrey Fudin

**"Fudin Factor"**  
A Methadone Conversion Formula

$$\text{Methadone (mg)} = \frac{X}{21} \left\{ 5.7 - 3 \sin \left( \frac{90}{\left( \frac{110}{X} + 1 \right)} \right) - \sin \left( \frac{90}{\left( \frac{320}{X} + 1 \right)} \right) \right\}$$

Let X= Morphine (mg)

Less exact to data from Ripamonti, et al 1998, more flowing and more likely in real life



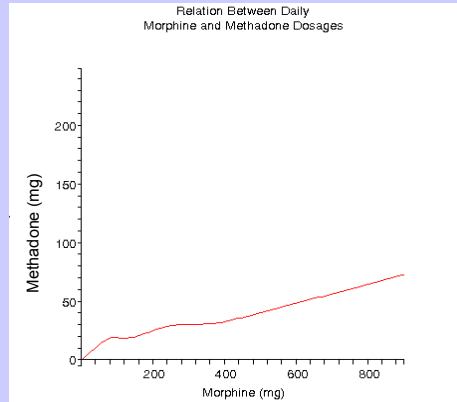
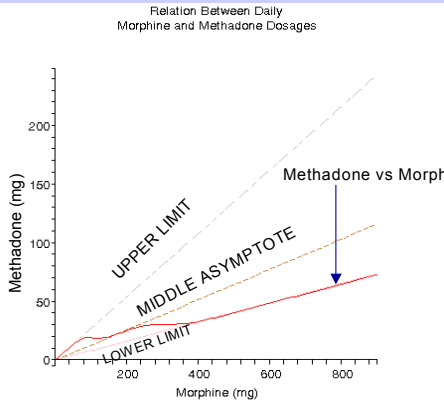
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$$\text{Methadone (mg)} = \frac{X}{21} \left\{ 5.7 - 3 \sin \left( \frac{90}{\left( \frac{110}{X} \right)^5 + 1} \right) - \sin \left( \frac{90}{\left( \frac{320}{X} \right)^7 + 1} \right) \right\}$$

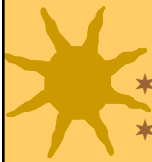
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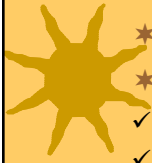
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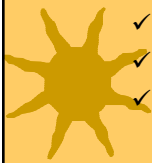
## Methods



★ The search criteria : January 1<sup>st</sup> 2003 to March 30<sup>th</sup> 2005.



★ 3396 methadone Rx were identified involving 446 veterans.



★ Each patient was patient was de-identified.

★ Each patient’s medical record was reviewed for:

✓ patient age

✓ gender

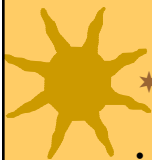
✓ an indication for opioid therapy, opioid medications,

✓ dose

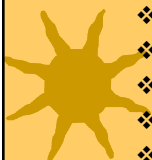
✓ pain score and adverse effects due to opioid treatment.



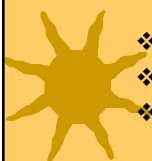
## *Exclusion criteria*



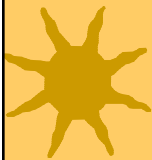
★ About 285 veteran medical records were reviewed for inclusion and exclusion.



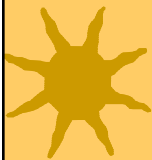
- The following records were excluded:
  - ❖ hospice patients
  - ❖ medical records with no pain evaluations
  - ❖ patients who were initially started on methadone prn use
  - ❖ patients who were started on methadone with other opioid simultaneously
  - ❖ records with an unusually high dose of methadone
  - ❖ patients whose failed opioid urine or serum drug tests
  - ❖ patients who were on methadone therapy without a specified indication for therapy.



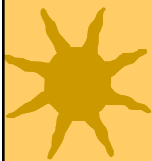
## *Methods..*



★ 100 veteran medical records were deemed qualified to be included in the study.



★ Veteran's non-methadone opioids were converted to morphine equivalence based on AHCPR Practice Guideline.\*



★ A conservative approach was taken when fentanyl patch was converted to morphine equivalence. 25mcg of fentanyl patch was converted to 45 mg morphine equivalence.

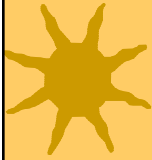
★ The total dose of morphine equivalence a veteran was receiving was compared to the "Fudin Factor" comparison table, the value in the Fudin factor table was recorded with any deviation from the Ripamonti's original table.

\*Jaxox A, Carr B, Payn R, Berde CB, et al: Management of Cancer Pain, Clinical Guidelines No. 9 ( AHCPR Publication No 94-0592) (p. 53)

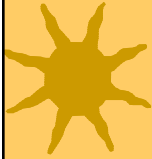


## *Methods*

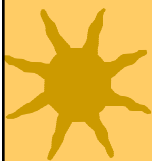
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★ The morphine equivalence dose was compared to the dose of methadone a patient was started on when he was switched from other opioids to methadone.



★ The final methadone dose patient received after titration was evaluated.

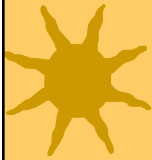


★ Adverse events and pain scale were also evaluated

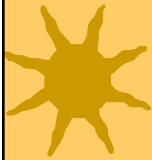


## *Results*

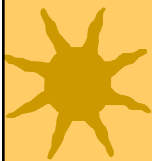
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★ The average age was 54 .4 years.



★ Only 13% of the veterans were females.

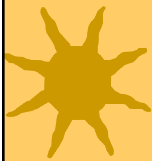
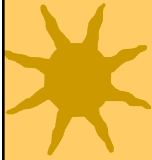
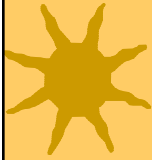


★ More veterans were on opioid therapy for chronic back pain and degenerative joint disease.

★ About 38% of veterans had 3 or more indications for therapy, 62% of veterans had 1 or 2 indications.



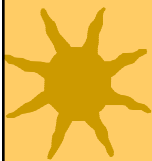
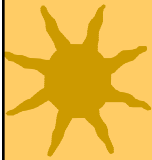
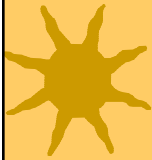
## *Method / Analysis*



- ★ Before patients were switched to methadone the following is the distribution of different opioids patients were receiving:
- ★ Fentanyl patch = 24
- ★ Morphine = 17
- ★ Hydrocodone = 23
- ★ Oxycodone = 51
- ★ Codeine = 2
- ★ Levorphanol = 1



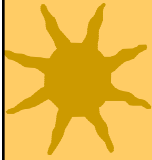
## *Results / Analysis*



- ★ About 18 patients were receiving 2 different opioids before they were switched to methadone.
- ★ There were no correlation between patient's pain scale and the amount of opioid they were receiving.
- ★ There was no difference in pain scale before patients were switched to methadone and after they were switched.
- ★ Some patients saw a slight improvement in pain control but did not translate to their pain rating at the time of reporting.
- ★ About 8 patients needed a breakthrough medication

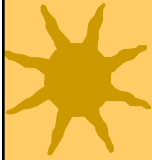


## Results / Analysis



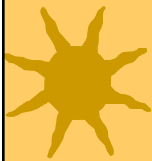
### \* *Indication for therapy and No. Veterans*

- \* Chronic back pain = 38
- \* DJD = 36
- \* Joint Pain = 18
- \* Osteoarthritis = 16
- \* Diabetic Neuropathy = 12
- \* Spinal Stenosis = 5
- \* Cervicalgia = 8
- \* Periph. Neurop. = 3
- \* Cancer Pain = 2

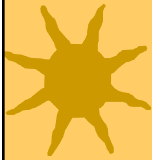


### \* *Adverse events :*

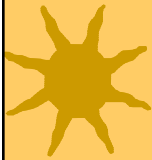
- constipation = 72%
- drowsiness and excessive daytime somnolence = 12%.
- Only 10% reported nausea at the onset of therapy apy.
- ❑ **There did not appear to be safety or adverse event concerns when patient's were converted to methadone.**



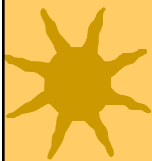
## Results / Analysis



\* The titration period between the first day of methadone therapy to final methadone dose ranged from 1 day to 120 days.



\* The median titration period was 30 days.

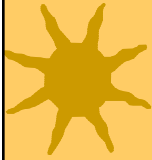


\* The titration period reported in the veteran's medical record could not be relied upon.

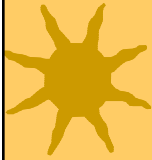




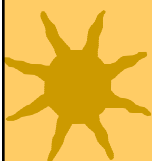
## *Conclusion / Discussion*



- \* The higher the dosage of the opioid being converted to methadone, the lower the conversion methadone dose that should be used.



- \* When switching from any opioid to methadone, use low dose methadone initially

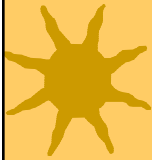


- \* In about 88% or higher opioid doses, the methadone dose calculated by the Fudin method was less than the actual dose prescribed.

- \* This indicates that the Fudin factor offers a potentially safer alternative than haphazard dosing equivalents used by many practitioners.



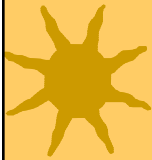
## *Confounding Factors*



- \* About 55% of veterans were on other pain modifying medications.

- \* Some of these SSRIs, TCA, clonidine, gabapentin, muscle relaxants, COX1/COX-2 inhibitors, tramadol, anticonvulsants. etc.

- \* These medications modify pain threshold to some extent depending on patient's comorbidities.

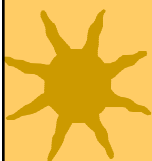


- \* Some veterans confuse emotional pain with physical pain.

- \* Some veterans report that their pain is usually better at home .

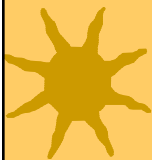
- \* Point of care pain score recorded in veteran's medical record not reflective of patient's normal daily pain.

- \* Therefore, it is difficult to use this data to validate the proposed tool for methadone conversion.

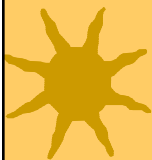




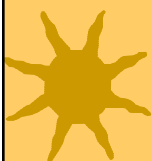
## *Ideas for Prospective study*



\* To be able to really assess patient's pain control to the amount of opioid being prescribed



\* An intensive telephone follow-up should be made to the patients at their homes.



\* ascertain their quality of life in relation to their pain level in their normal environment

\* All relevant conversation must be diligently documented so that it is analyzed for later pain evaluations.

\* This study should be used as groundwork toward a prospective study to validate the proposed Fudin factor .

## *References*

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[www.paindr.com](http://www.paindr.com) last visited – January 31<sup>st</sup> 2005

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