Improving Existing Treatments by Understanding Brain Processes Underlying Behavior

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Who am I and How did I get where I am?

- Interest in changing health behavior
- Trained in systems neurobiology, cell biology, pharmacology and anatomy
  - Research focus in stress, pain and opioid systems
- Taught at medical school, found neuroscience research findings were rarely used
- Turned to health services research to study how to change health care and health care systems to fit with what we know about how the brain works and thus people behave.

Strategy

- Reexamine clinical problems and clinical perspectives on how to address them by considering relevant neuroscience data on the problem and its treatment.
- Hypothesis: Bringing a non-clinical perspective onto clinical problems in behavioral health may resolve clinical controversies and identify new methods to address issues.
- Areas of interest
  - Treatment of substance use disorders, particularly opioid use disorders
  - Use of opioids for the treatment of chronic pain
  - Effects of psychosocial treatments on health behavior
  - Use of data and technology to modify clinical behaviors

Setting

- United States Veterans Health Administration
- Federally-funded national system of health care facilities to provide health care to qualifying military Veterans
- 141 health care systems providing care at over 1500 sites
- ~5.6 million unique patients seen per year
- National office sets and implements policy for all facilities
- National research program focuses on improving care for high impact conditions in the Veteran population

EXAMPLE 1: OPIOID PRESCRIBING FOR CHRONIC PAIN IN PRIMARY CARE

- Highly prevalent:
  - 18% of VA patients have an opioid prescription in a given year. Roughly 40% of prescriptions are chronic (more than 90 days in the year).
- Problems with adverse events:
  - Opioid overdose has nearly overtaken auto accidents as the primary cause of accidental death in the U.S.
- Lack of data on long-term efficacy of opioids for chronic pain conditions
  - Almost no research on effectiveness of opioid medication for pain beyond 12 weeks.

Clinical Practice guidelines

- VA/DoD Clinical Practice Guidelines for Opioid Therapy for Chronic Pain (2003, 2010)
- Provide expert consensus based recommendations regarding care practices to reduce risk and improve effectiveness of opioid therapy
  - Examples:
    - Routinely conduct urine drug screens for illicit substances and opioid medications before prescribing
    - Only prescribe opioids to patients with active substance use disorder if they are receiving SUD treatment
- But guideline recommendations are poorly followed in primary care practice

Why?

- Providers say:
  - Not enough time
  - Not educated in pain management
  - Patients make them uncomfortable or scared
    - Suggest that patients bully them into giving medications
    - Feel threatened and driven to prescribe
    - But also scared of legal ramifications of prescribing
- Providers don't know what to do, have plenty of other useful things they could attend to instead, and don't like interactions with pain patients

What do patients think about their care?

- Patients often say:
  - They want to keep their prescriptions going, even though their pain severity scores remain high when on them
  - Doctors don't listen, just give them pills
  - Don't want to refuse pills because clinician seems so excited about them
  - Like to share with family and friends so that they can help others with their pain

  - Among a sample of ~200 patients receiving opioids from their primary care clinician, oversampled for mental health risk factors associated with misuse, over a third reported under-using or not using their opioid prescription.

Why Might clinicians prescribe opioids often and carelessly ?

- Neuroscience findings emphasize that:
  - Observing people in pain activates neural pain pathways similar to being injured yourself
    - Being around people in pain is painful
  - Reducing on-going pain activates reward circuits and is reinforcing
    - People will be drawn to repeat behaviors that immediately reduced activity in neural pain pathways previously
  - Stress increases the value of or drive to obtain immediate rewards
    - When one is stressed or in pain, they will be highly driven to get relief immediately

Implications

- Providers should find pain patients painful to be around, and be subconsciously and powerfully driven to find a way to immediately reduce their pain or get them to leave.
- Suggests that if clinicians find writing opioid prescriptions reduces patients' distress or ends the visit, opioid prescribing could become rewarding and habitual to the provider.
- Suggests that opioid prescribing decisions may be highly emotionally driven.
- This would suggest that interventions that effectively address habits rather than lack of knowledge may be needed to improve prescribing.

A DIFFERENT PERSPECTIVE?

- Clinical perspective suggested:
  - More training for primary care clinicians
  - Providing more time with patients
  - Developing methods to screen out "problem" patients
- Neuroscience perspective suggested:
  - Use of methods to address clinicians' prescribing "habit"
    - Slow down prescribing decisions
    - Make it more difficult to prescribe
    - Make prescribing less rewarding
    - Increase salience of longer-term risks of prescribing
    - Provide more effective alternatives for providing patients with short-term relief
- Change the system rather than ask the patients and providers to act in opposition to their behavioral drives

How might we improve opioid therapy guideline adherence?

- Focus on system-level interventions rather than focusing on teaching providers what to do.

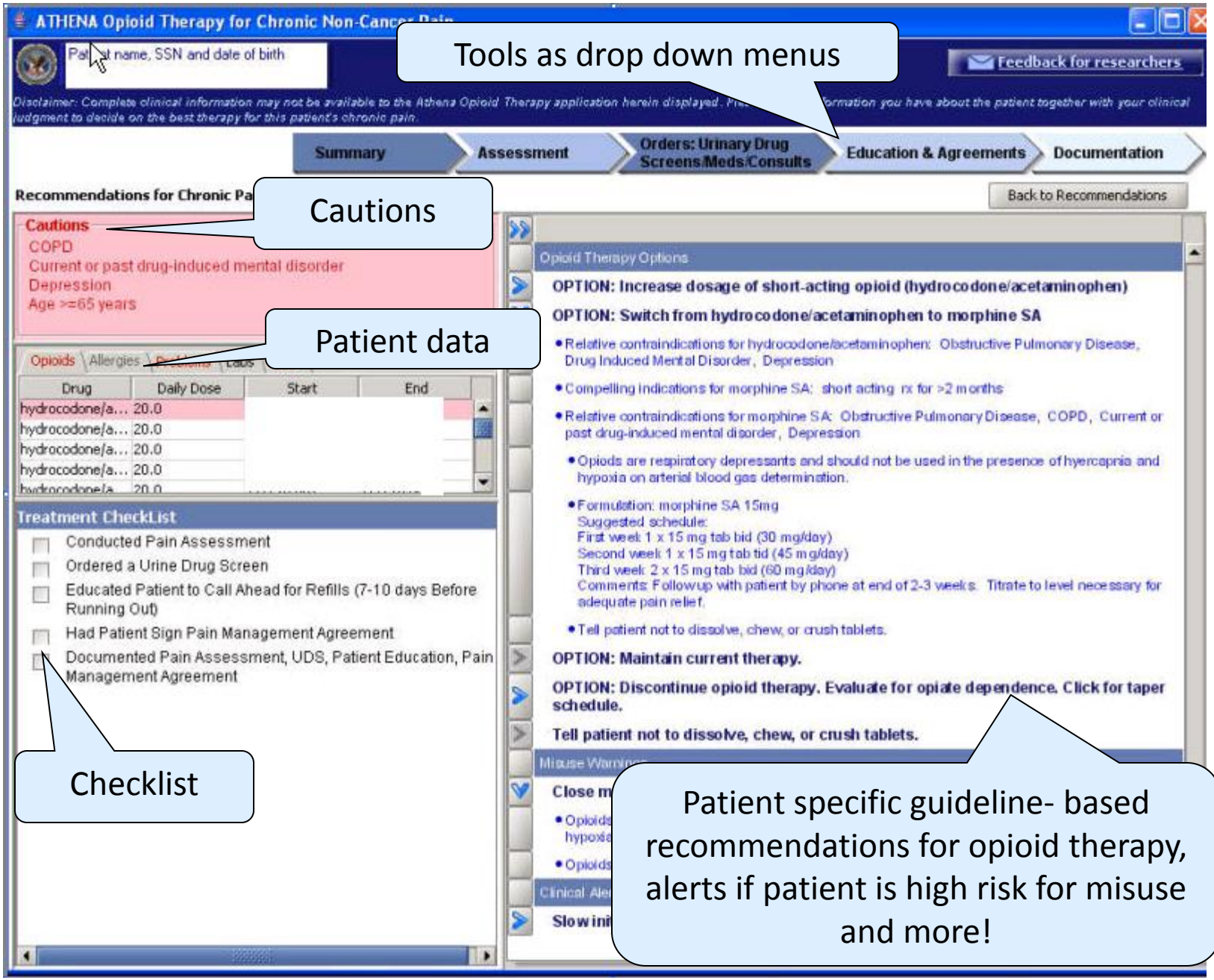
- Example 1: Develop computerized decision support systems to help primary care clinicians with opioid prescribing
  - Make it easier for clinicians to follow guideline recommendations, and harder to ignore them.

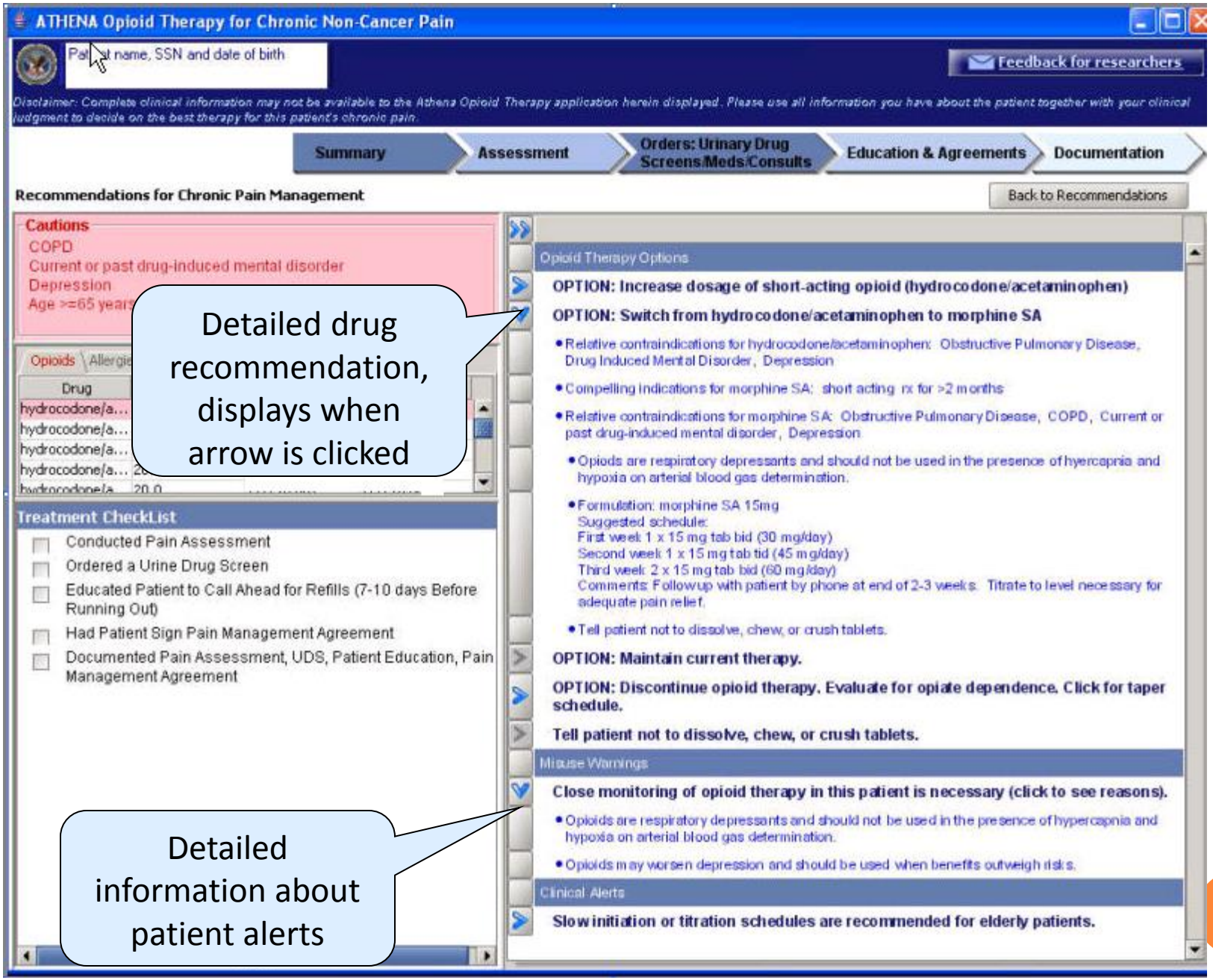
GOALS OF COMPUTERIZED DECISION SUPPORT

- Tell clinicians what to do
  - Address lack of knowledge
  - Reduce discomfort around saying no by reducing clinician ownership of the decision
- Make it easier to do what they are supposed to do
  - Streamline good practice processes
  - Provide reminders and detailed instructions about how to follow good practices in the local setting
  - Provide information to prioritize good practice processes
    - For example, warning about specific patient risks, alerts when a patient has an opioid prescription
- Make it harder to do risky prescribing practices
  - Increase conflict around taking clinical short-cuts, by alerting clinicians of reasons why that might be risky

ATHENA-OPIOID THERAPY Decision Support System

- Features include:
  - Patient specific recommendations
    - Warnings about patients at high risk for misuse
    - Specific drug dosing recommendations
  - Highlighted opioid therapy-relevant patient information
  - Checklist of good clinical practices
  - Standardized pain assessment with write-back to medical record
  - Tools
    - Patient education materials
    - Drug conversion calculator
    - Referrals for mental health & behavioral treatments, exercise programs and self-help
    - Guidelines for use of non-opioid pain medications
    - Suggested responses to aberrant medication use behaviors


ATHENA Opioid Therapy for Chronic Non-Cancer Pain
Patient name, SSN and date of birth
Feedback for researchers
Disclaimer: Complete clinical information may not be available to the Athena Opioid Therapy application herein displayed. Please use the information you have about the patient together with your clinical judgment to decide on the best therapy for this patient's chronic pain.
Summary
Assessment
Orders: Urinary Drug Screens/Meds/Consults
Education & Agreements
Documentation
Recommendations for Chronic Pa
Back to Recommendations
Cautions
COPD
Current or past drug-induced mental disorder
Depression
Age >=65 years
Opioids
Allergies
Drug
Daily Dose
Start
End
hydrocodone/a... 20.0
hydrocodone/a... 20.0
hydrocodone/a... 20.0
hydrocodone/a... 20.0
Treatment CheckList
Conducted Pain Assessment
Ordered a Urine Drug Screen
Educated Patient to Call Ahead for Refills (7-10 days Before Running Out)
Had Patient Sign Pain Management Agreement
Documented Pain Assessment, UDS, Patient Education, Pain Management Agreement
Opioid Therapy Options
OPTION: Increase dosage of short-acting opioid (hydrocodone/acetaminophen)
OPTION: Switch from hydrocodone/acetaminophen to morphine SA
Relative contraindications for hydrocodone/acetaminophen: Obstructive Pulmonary Disease, Drug Induced Mental Disorder, Depression
Compelling indications for morphine SA: short acting rx for >2 months
Relative contraindications for morphine SA: Obstructive Pulmonary Disease, COPD, Current or past drug-induced mental disorder, Depression
Opiods are respiratory depressants and should not be used in the presence of hyercapnia and hypoxia on arterial blood gas determination.
Formulation: morphine SA 15mg
Suggested schedule:
First week: 1 x 15 mg tab bid (30 mg/day)
Second week: 1 x 15 mg tab tid (45 mg/day)
Third week: 2 x 15 mg tab bid (60 mg/day)
Comments: Followup with patient by phone at end of 2-3 weeks. Titrate to level necessary for adequate pain relief.
Tell patient not to dissolve, chew, or crush tablets.
OPTION: Maintain current therapy.
OPTION: Discontinue opioid therapy. Evaluate for opiate dependence. Click for taper schedule.
Tell patient not to dissolve, chew, or crush tablets.
Tools as drop down menus
Patient data
Checklist
Patient specific guideline- based recommendations for opioid therapy, alerts if patient is high risk for misuse and more!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Detailed drug recommendation, displays when arrow is clicked
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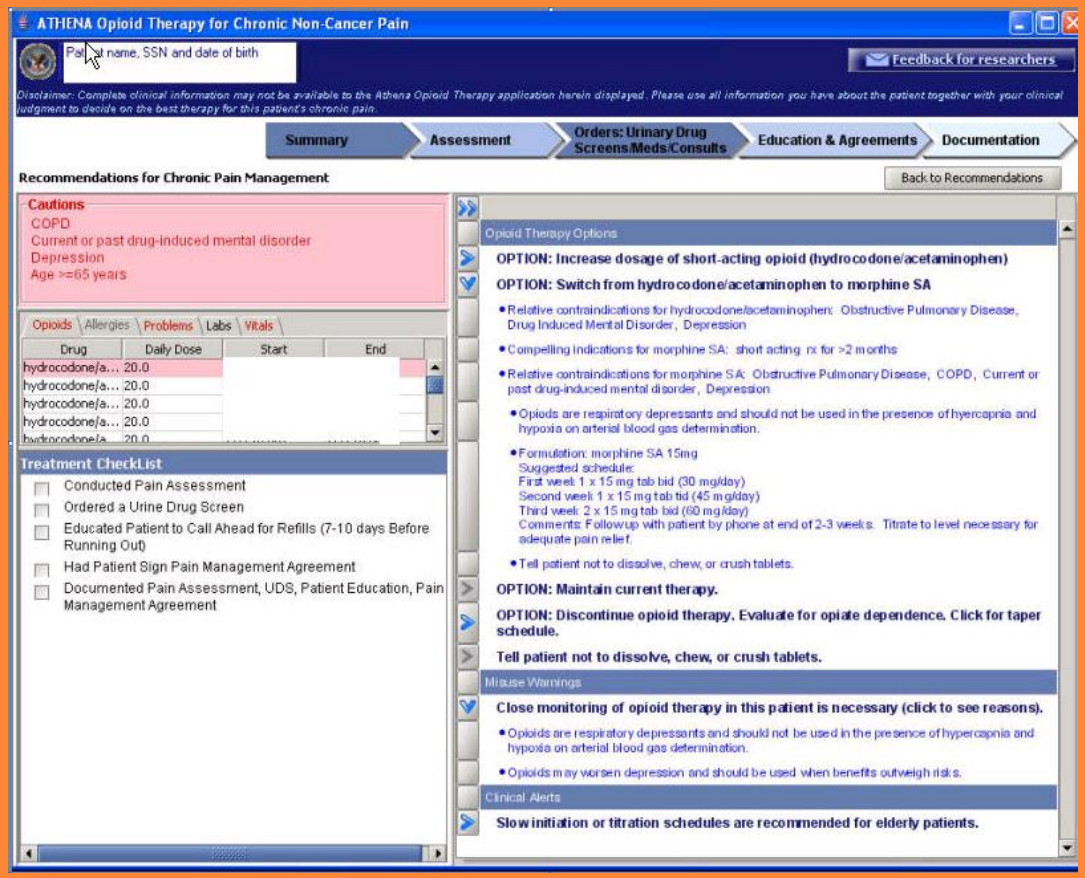
OPTION: Maintain current therapy.
OPTION: Discontinue opioid therapy. Evaluate for opiate dependence. Click for taper schedule.
Tell patient not to dissolve, chew, or crush tablets.
Misuse Warnings
Close monitoring of opioid therapy in this patient is necessary (click to see reasons).
Opioids are respiratory depressants and should not be used in the presence of hypercapnia and hypoxia on arterial blood gas determination.
Opioids may worsen depression and should be used when benefits outweigh risks.
Clinical Alerts
Slow initiation or titration schedules are recommended for elderly patients.

IF PATIENT IS ON OPIOIDS, WINDOW POPS UP IN FRONT OF ELECTRONIC MEDICAL RECORD

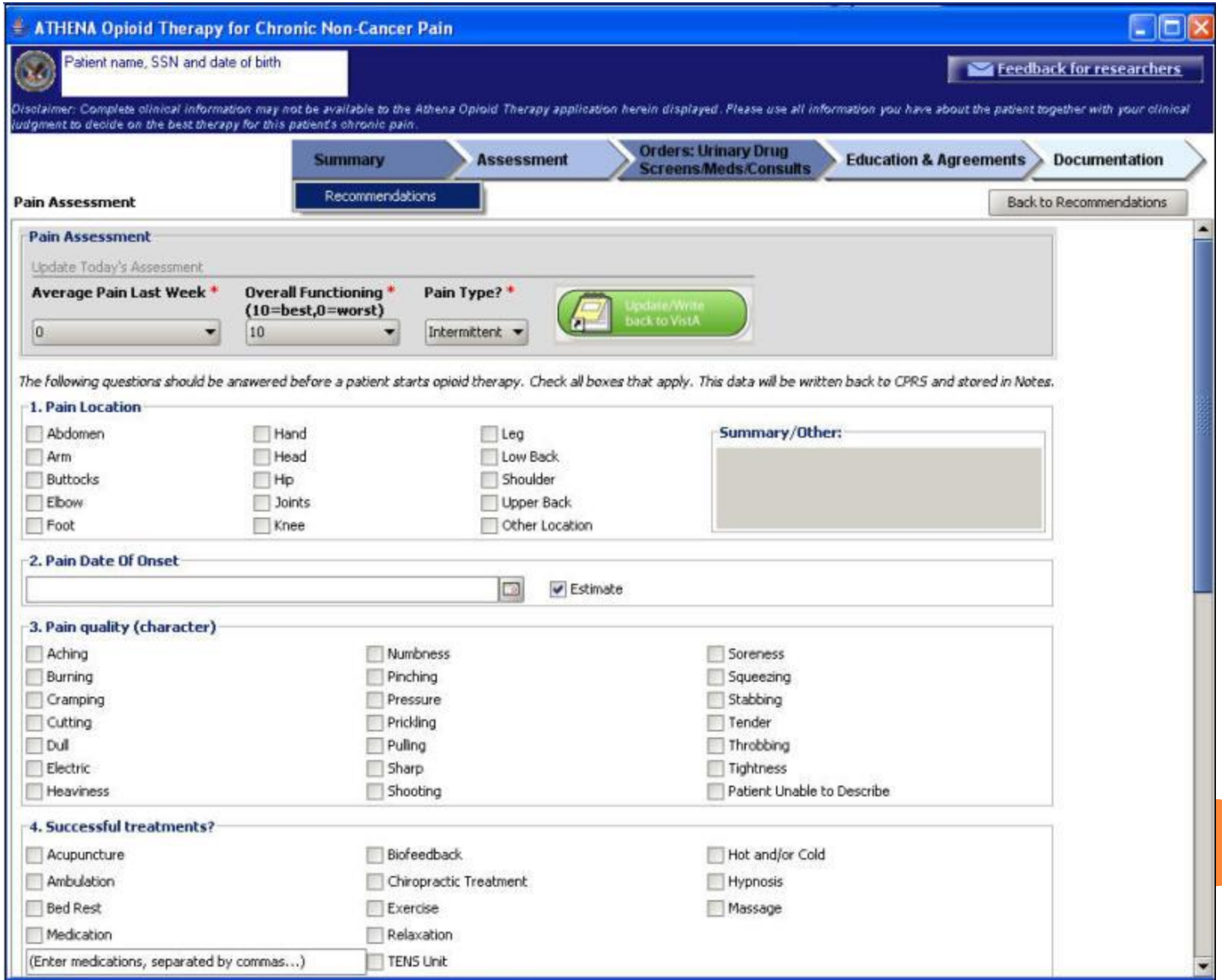
Electronic Medical Record



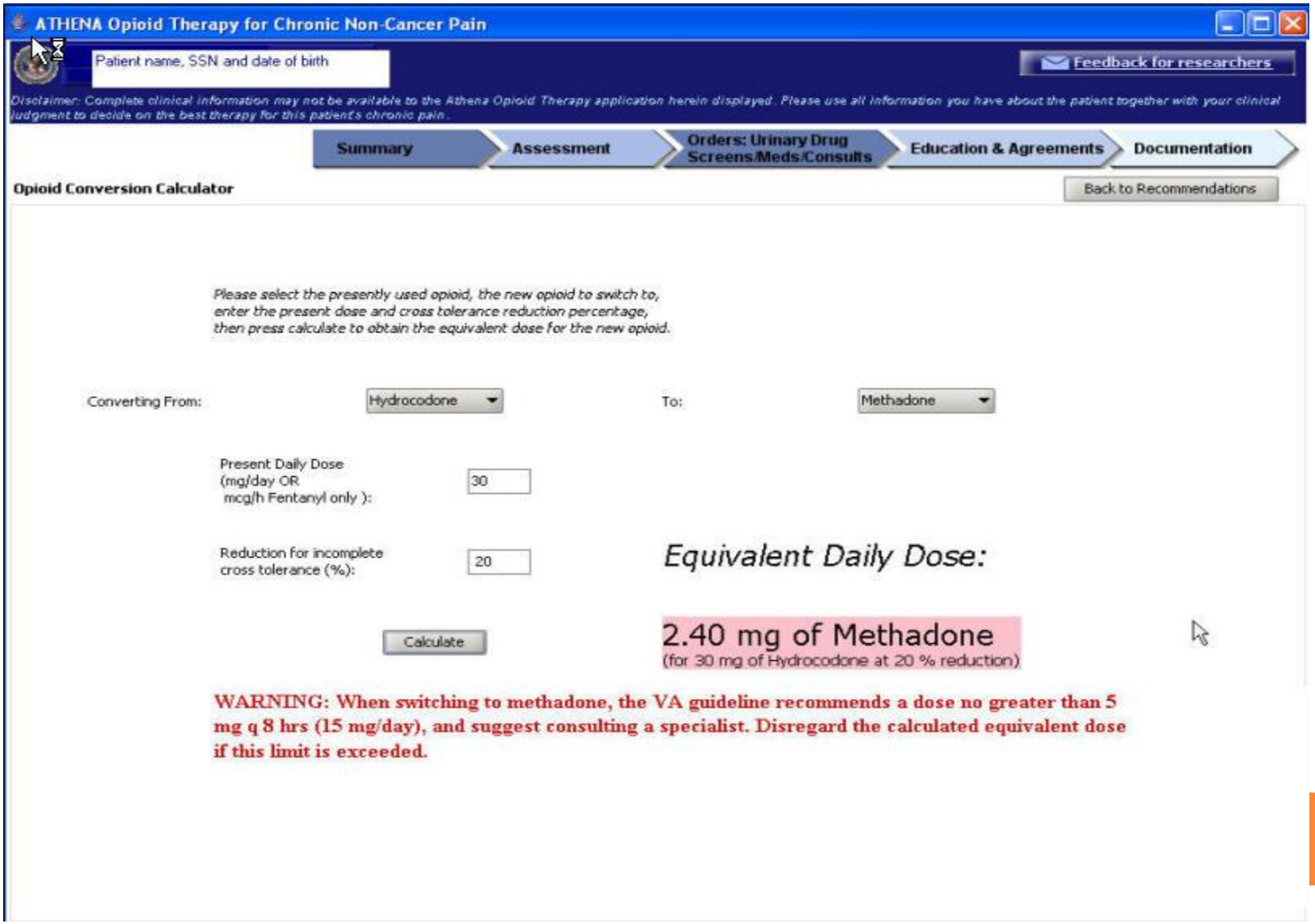
STAMP DISPLAY FOR PATIENT NOT ON OPIOIDS. IF YOU CLICK ON BOX YOU GET FULL DISPLAY WITH ALL RECOMMENDATIONS

Electronic medical record window

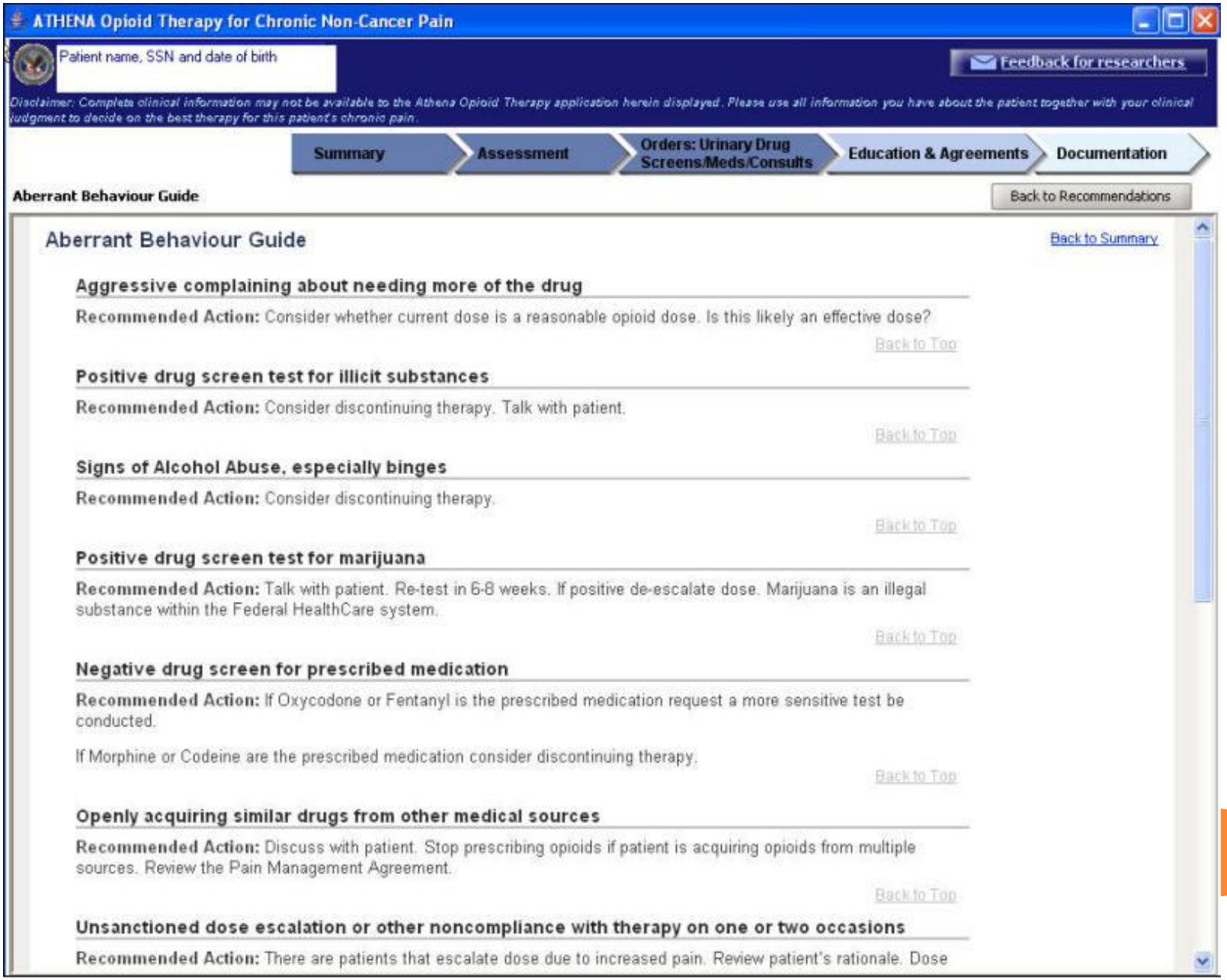
PAIN ASSESSMENT TOOL, IS WRITTEN BACK TO ELECTRONIC MEDICAL RECORD AS A NOTE



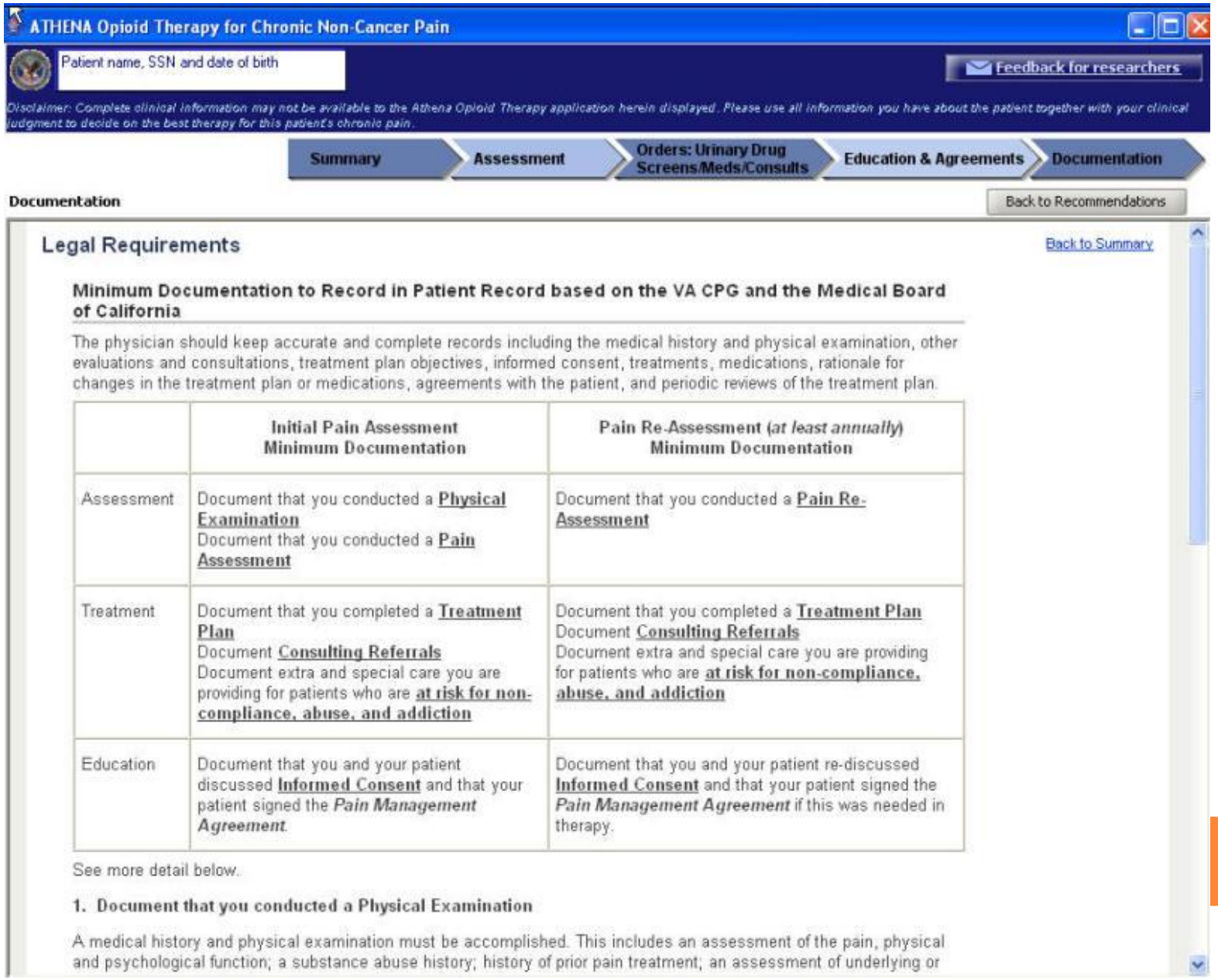
Conversion calculator tool



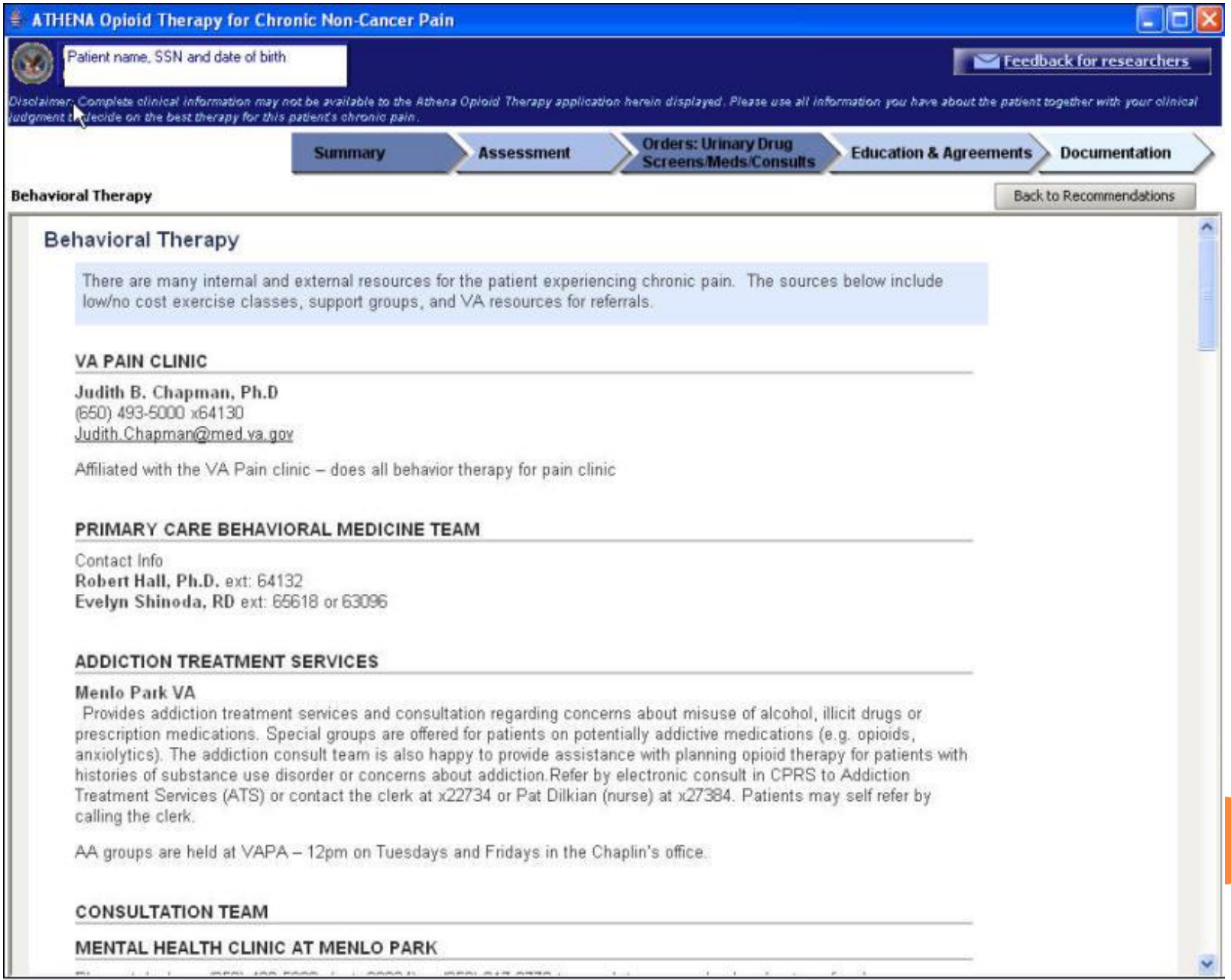
Aberrant Behavior Guide tool



Legal requirements to be met when prescribing opioids



BEHAVIORAL THERAPY REFERRALS WITHIN AND OUTSIDE VA



System Rated Highly Usable

Table 1: System Usability Scale:

	Round 1		Round 2	
	mean	**sd**	**Mean**	**sd**
1. I think that I would like to use this system frequently	2.75	0.50	3.25	0.96
2. I found the system unnecessarily complex	2.50	1.11	3.00	0.00
3. I thought the system was easy to use	3.00	0.76	3.25	0.50
4. I think that I would need the support of a technical person to be able to use this system	3.50	1.51	4.00	0.00
5. I found the various functions in this system were well integrated	2.50	0.82	3.00	0.82
6. I thought there was too much inconsistency in this system	3.25	0.98	3.75	0.50
7. I would imagine that most people would learn to use this system very quickly	3.25	0.69	3.00	0.00
8. I found the system very cumbersome to use	2.75	1.11	3.75	0.50
9. I felt very confident using the system.	3.00	0.53	3.25	0.50
10. I needed to learn a lot of things before I could get going with this system	3.25	1.27	3.75	0.50
Overall Score:	74.38		84	p=0.0167

But mostly used by clinicians who were already relatively attentive to following good opioid prescribing practices!

NEED TO GET USE OF GOOD OPIOID PRESCRIBING PRACTICES PRIORITIZED

- Decision support and process redesign can streamline and facilitate good practice, but only among those willing to attend to pain and opioid management.

- Need supervisory or administrative assistance and pressure to motivate clinicians to take the time and effort to use good prescribing practices.

How might we improve opioid therapy guideline adherence?

- A performance measurement system can help bring attention to current practice problems and help clinicians and administrators tell when practice is improving.
  - Identify variation in clinical practice and targets for quality improvement
  - Monitor impact of quality improvement efforts over time
- Can help link consequences of prescribing short-cuts to the immediate prescribing practice.

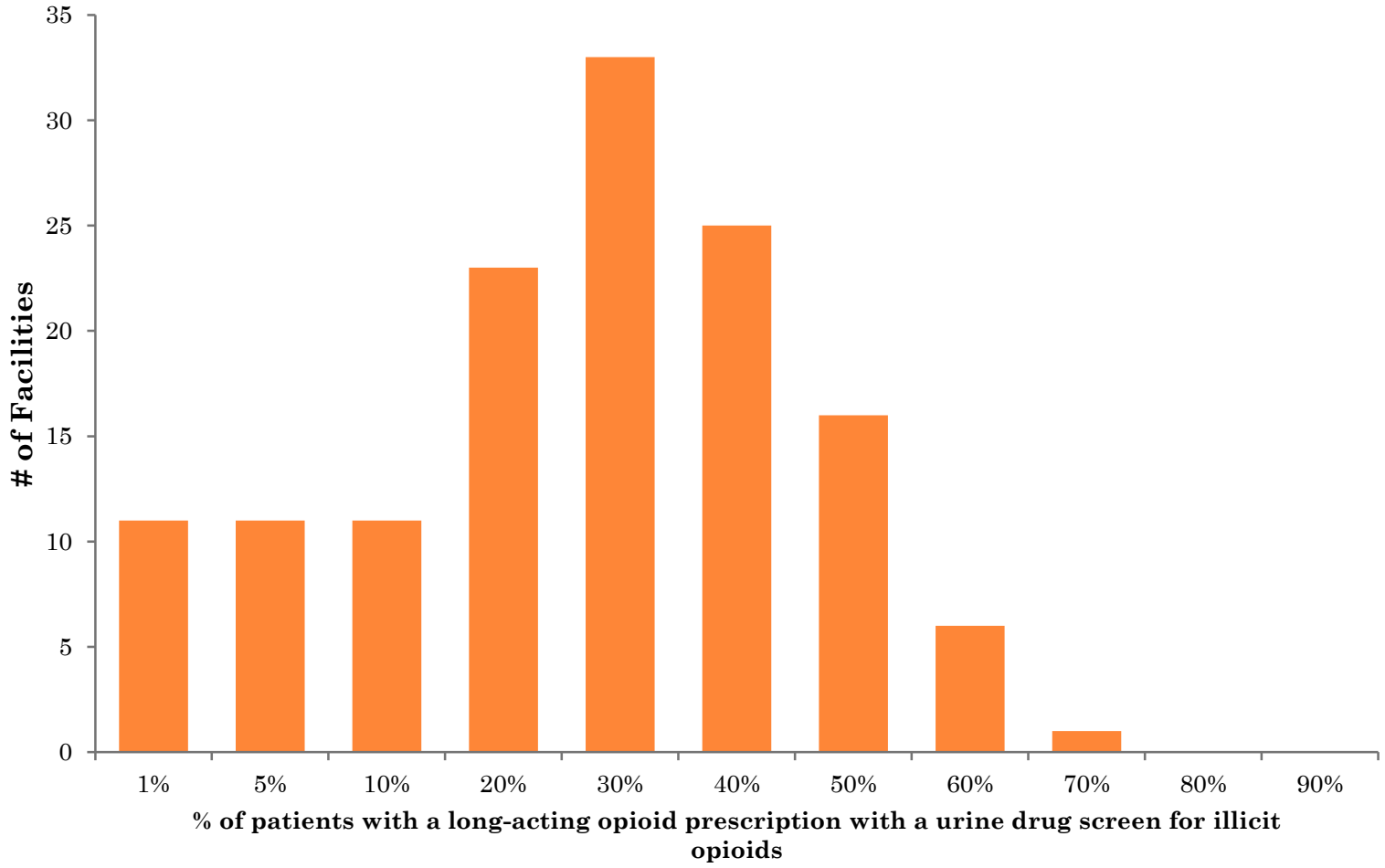
DEVELOPED A SUITE OF ADMINISTRATIVE DATA BASED METRICS TO ASSESS ADHERENCE TO CLINICAL GUIDELINE RECOMMENDED PRACTICE

- Identified practices in key domains that could be identified in "billing" data
- Developed measures of practice or outcome in these domains
- Creating a data report to allow facilities to track their performance on these measures with quarterly updates. Allow comparison to national performance and performance at other facilities.
- Identify model programs.
- Target and evaluation quality improvement efforts.

Measure domains

- Side Effects Management
- Serious adverse effects
- Dangerous Drug Interactions
- Minimizing Misuse Risk
- Appropriate Follow-Up
- Avoidance of Sole Reliance on Opioids
  - Psychosocial treatments
  - Other pharmacotherapies
  - Rehabilitation medicine
  - Complementary and alternative medicine treatments
- Absolutely Contra-Indicated Opioid Prescriptions
- Medication Management/Pharmacy Reconciliation
- Ordering of Appropriate Lab Tests

Examine current practice and identify areas and sites for quality improvement



EXAMPLE 2: METHADONE MAINTENANCE TREATMENT

- Clinic-level surveys of methadone maintenance clinics indicated wide variation in both mean and individual doses provided to clients.
- Some suggested that this was evidence of poor practice as randomized controlled trials indicated that higher doses (e.g. 60-100mg/day) produced better patient outcomes than lower doses (e.g. under 60mg/day).
- But clinicians reported that many patients do well on low doses.

Need for improvement?

- VHA was interested in conducting quality improvement in hopes of improving substance use outcomes for opioid dependent patients. Did dosing practices require improving? Or did patient needs vary by site?

Neuroscience on effects of methadone maintenance

- Substantial tolerance to opioids develops rapidly through a variety of mechanisms, depending partially on the pattern of drug exposure and withdrawal experienced over time
- At relatively low dose, methadone will prevent or minimize withdrawal symptoms in opioid dependent subjects.
- At higher doses, methadone will act as a competitive antagonist at mu opioid receptors – blocking the acute effects of fast-acting opioid drugs, like heroin.

Does methadone dose matter for patient outcome?

- Conducted an 8 site prospective observational study of new patient outcomes in the first year of treatment at VA methadone maintenance clinics.
- Clinics were selected such that half had relatively low mean methadone doses, and half had relatively high mean methadone doses
- Found no association between patient-level methadone dose and substance use outcomes.
- But patients at the 4 clinics with relatively low mean methadone dose had poorer substance use outcomes than those at the 4 clinics with relatively high mean methadone dose.

Did dose matter or not?

- Examined methadone dosing in patients who achieved abstinence versus overall clinic dosing at low and high dosing clinics.
- Examined factors associated with higher methadone dosing among patients who achieved abstinence.

Effective methadone dose varies substantially at the individual level

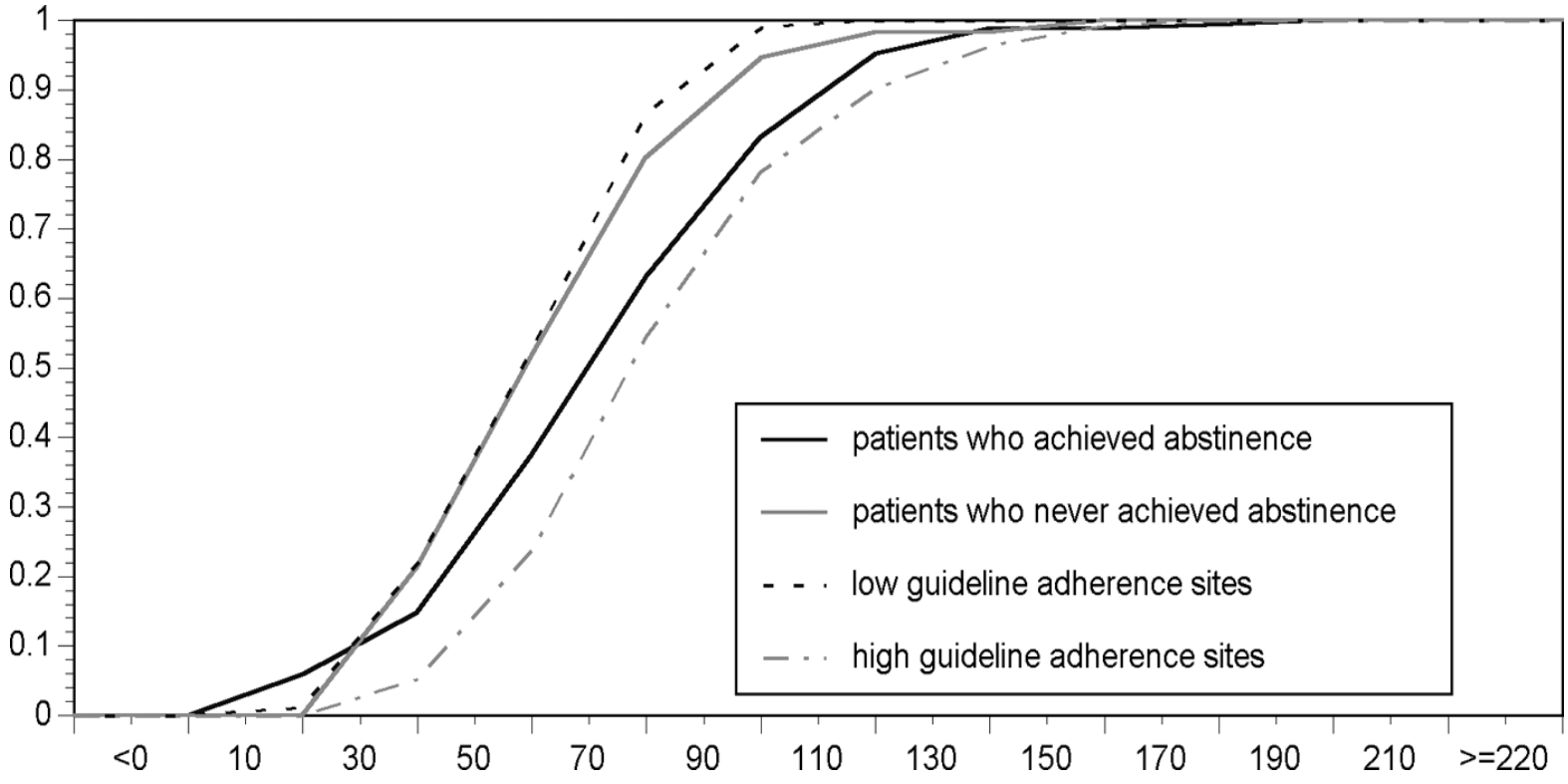


Figure 1. Cumulative Dose Histogram Depicting the Proportion of Patients at or below a Given Methadone Dose (in mg)

Predictors of methadone tolerance.

- Created a model looking at associations between effective individual methadone dose and treatment clinic practices and patient factors.
- The model predicted 42.3% of the variance in the methadone dosage at which a patient maintained abstinence.
  - A PTSD dx increased dosage by 12.1 mg (95%CI: 3.4–20.8 mg).
  - A depression dx increased dosage by 14.1 mg (95%CI: 5.6–22.6 mg).
  - Each previous drug detoxification episode increased dosage which by 0.9 mg (95%CI: 0.1–1.7 mg).
  - For every 10% increase in local heroin purity, the dosage decreased by 4.0 mg (95% confidence interval: −6.8 to −1.2 mg).
  - Abstinent patients received 0.1 mg more (95% confidence interval: 0.06–0.14 mg) for each day they remained in treatment.
  - For each point increase on a counselor's tendency to encourage dosage reduction scale, dosage was 7.4 mg (95%CI: −10.5 to −4.2 mg) lower.

Conclusions

- Disorders linked to disruptions in endogenous opioid systems increase methadone dose needs.
- Exposure to drug withdrawal (e.g. by planned detoxification or use of less pure heroin) increases methadone dose needs.
- Tolerance builds with on-going methadone exposure.
- Doses can be minimized through counselor efforts, but this may limit patient recovery to those that are less tolerant.
- Factors identified as important for opioid tolerance in basic science studies appear clinically important in terms of patient methadone dose needs.

Conclusion

- Focusing on dosing process and use of an appropriate clinical endpoint rather than dose should optimize methadone maintenance treatment.

- Opioid dosing must be individualized based on co-morbidities, and history of opioid exposure and withdrawal.

Summary

- Non-clinician perspective can sometimes provide insight into clinical process and interventions to improve care.

- Multi-disciplinary research teams may be useful for addressing intractable or controversial clinical problems.

Acknowledgements

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