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## INTRODUCTION

Urine drug screening is a common strategy for monitoring adherence to chronic opioid therapy. The conventional use of this tool involves interpretation of the presence or absence of a drug. If specific doses of an opioid can be associated with a range of urine drug levels of adherent patients, the ability to interpret urine drug screening would be enhanced. A proprietary model that utilizes urine levels for monitoring adherence to specific prescribed chronic oxycodone regimens has been developed using data from a cohort of Wisconsin patients determined to be adherent to therapy. The model consists of two components: an algorithm used to adjust quantitative urine drug levels for hydration and lean body weight, and a set of reference ranges for adjusted urine drug levels.

## PURPOSE

The purpose of this study was to evaluate this model in a different population of adherent, oxycodone-treated patients than the population that was used to develop it.

## METHODS

A cohort of pain patients receiving stable oxycodone therapy was identified from a study at New York's Beth Israel Medical Center (BIMC). Investigators established adherence to opioid therapy using multiple criteria including:

1. Urine drug testing consistent with adherence. Patients were considered non-adherent if their urine drug sample was found to have the presence of illicit drugs or non-prescribed controlled medications, or lacked the presence of the prescribed opioid.

## METHODS Continued

2. Morisky Validity of Medication Adherence survey consistent with adherence. This four-item instrument evaluates the use of more or less medication than prescribed, assessing such factors as forgetting to take prescribed medication, carelessness about taking medications in a timely manner, stopping medication if experiencing less pain and taking more medication if pain intensifies.

3. Appropriate self-reported medication use compared to prescribed regimen. The review included medication dose, frequency, time and date of last dose and use of PRN medication.

Patients who were deemed adherent to prescribed therapy based on these criteria were considered candidates for this study.

To explore how the reference ranges perform across two different populations, the level of agreement between two methods of adherence assessment was determined. Urine drug levels using mass spectrometry were obtained from the cohort of Beth Israel patients, who were assessed as adherent using the methods outlined above, and these levels were adjusted for hydration and lean body weight using the proprietary algorithm. These adjusted urine drug levels were then compared to the pre-established reference ranges of urine drug levels from the adherent Wisconsin cohort.

## STATISTICS

The percentage of samples coming from patients in the Beth Israel study cohort whose adjusted urine drug level results fell within the reference ranges was determined and 95% exact binomial confidence intervals were calculated. The reference ranges established from the Wisconsin cohort were defined as

## STATISTICS Continued

$\pm 1.96$  standardized units of the observed adjusted urine drug level derived from a large database of patients determined to be adherent to therapy. To determine whether results varied based on the manner of prescribing, patients were divided into those who were prescribed a stable daily dose without flexibility in how they were to be taking their medications ("fixed dose") and those who were receiving a stable dose but were given the ability to modify their dosing based on variation in pain intensity ("variable dosing"). Results are reported for the entire sample and also separately for those patients receiving fixed or variable dosing, respectively.

## RESULTS

In total, 108 patients from the Beth Israel cohort provided 112 urine samples that were included for analysis. Samples came from 62 females and 46 males. Mean age was 52 years (range 24 to 78 years) Sixty-five percent were Caucasian, 18% were Black, 16% were Hispanic and 1% were other (Chart 1). Sixty samples were from patients taking a fixed total daily dose of oxycodone (28 females and 30 males) and 52 were obtained from patients on variable dosing regimens (34 females and 16 males) (Chart 2).

Of the total 112 BIMC samples, 99 or 88.4% (95% CI, 81%, 93.7%) had adjusted urine drug levels within  $\pm 1.96$  standardized units. For patients on fixed dose oxycodone, 54 of 60 or 90% (95% CI, 79.5%, 96.2%) of patients were within  $\pm 1.96$  standardized units; for those on variable dose oxycodone, 45 of 52 or 86.5% (95% CI, 74.2%, 94.4%) were similarly within the references ranges of  $\pm 1.96$  standardized scores (Table 1 and illustrated in Chart 3).

## RESULTS Continued

Chart 1

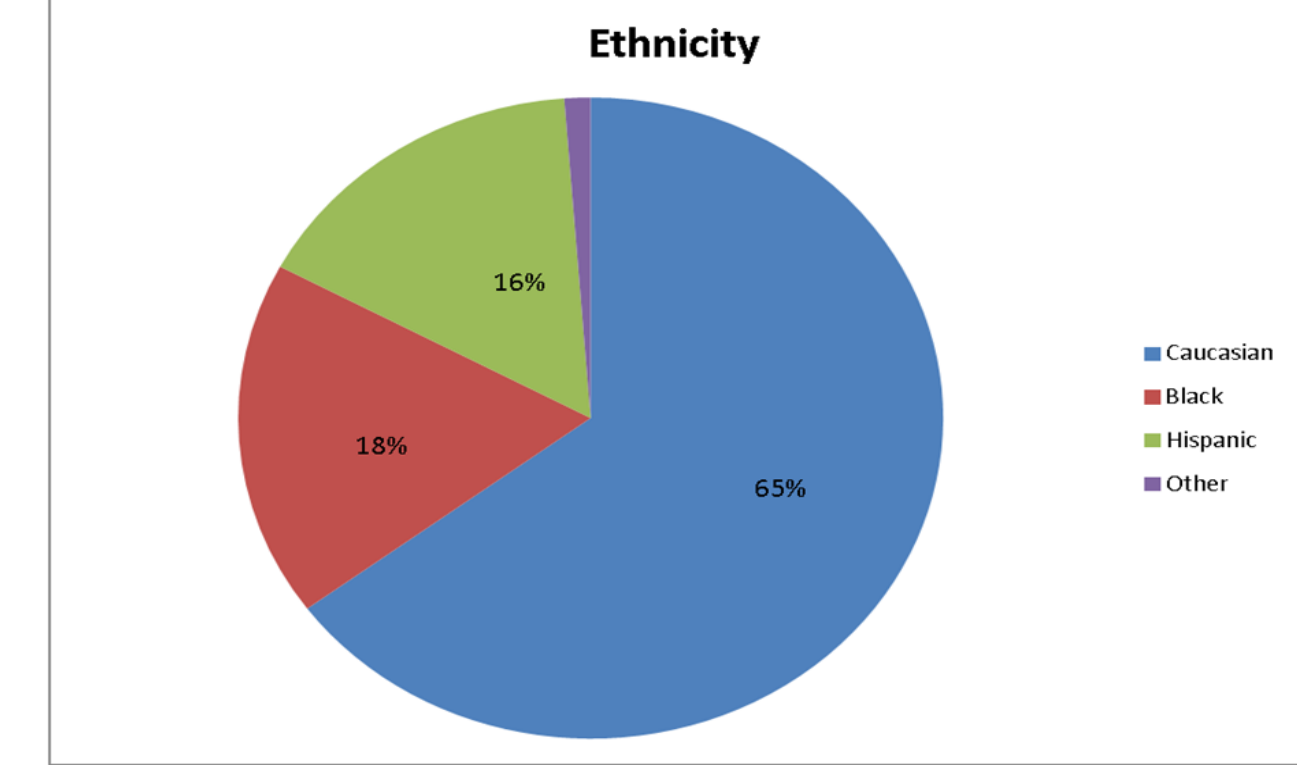


Chart 2

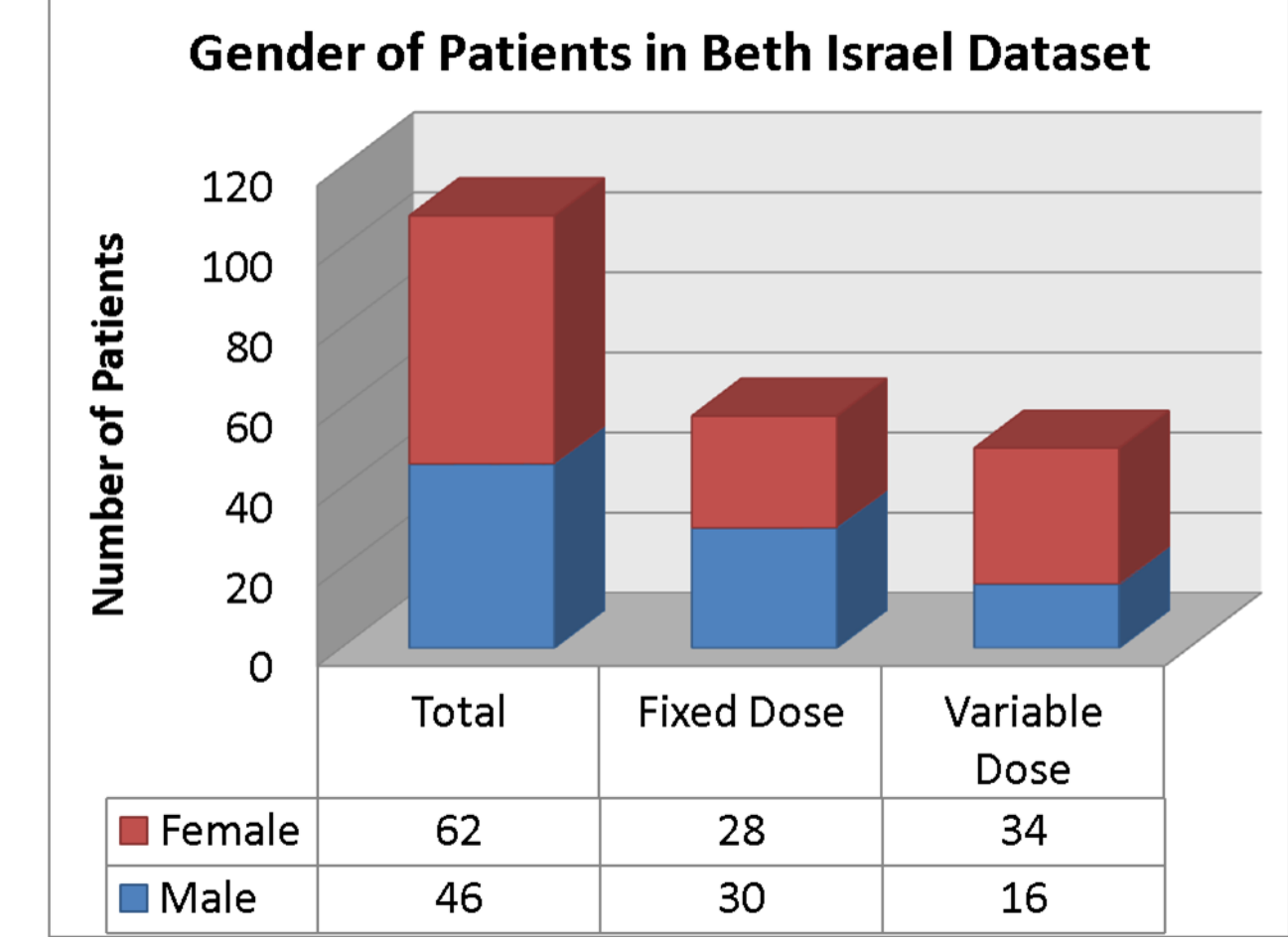
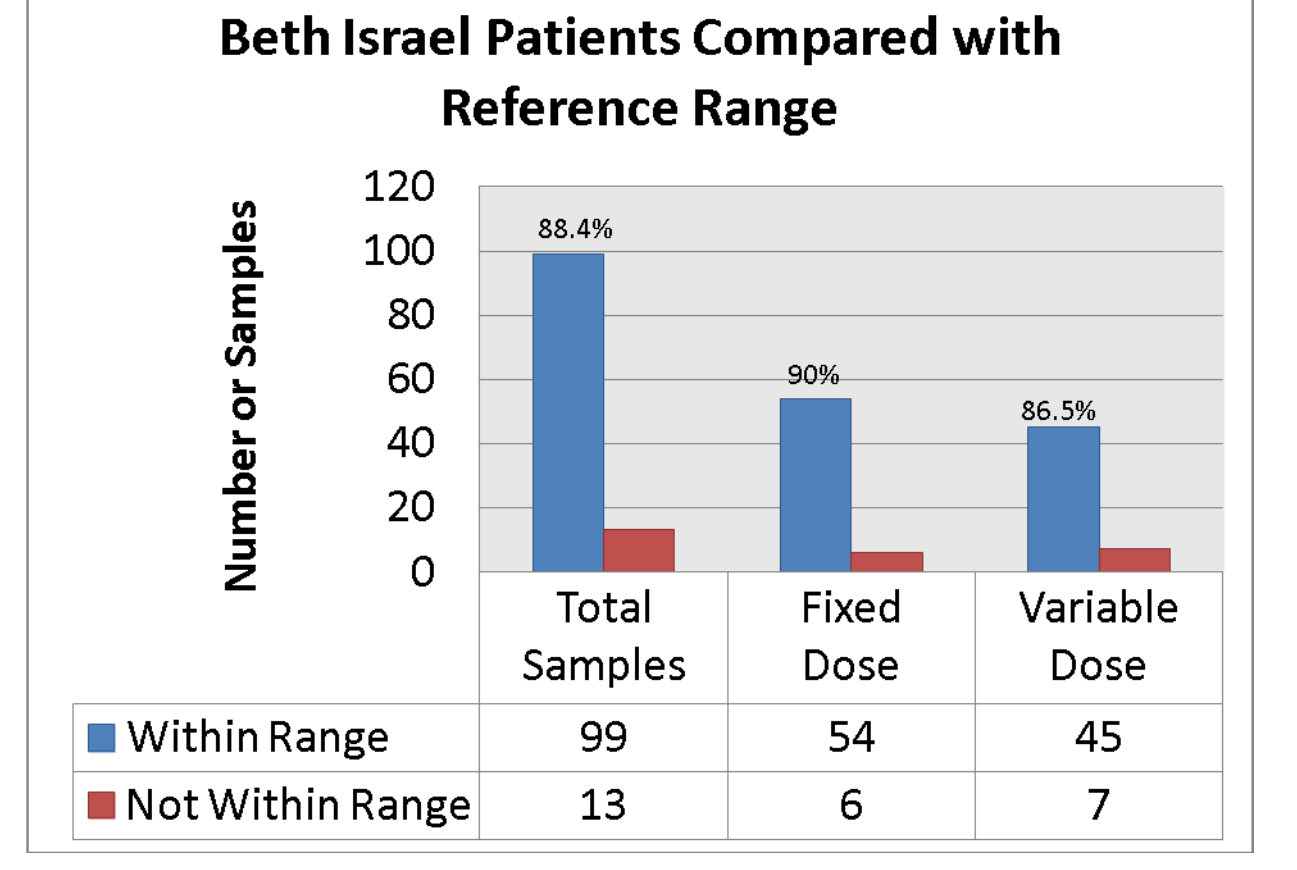


Table 1

Results					
	Patients	Samples	Samples within Reference Range	Percent of Samples within Reference Range	95% Confidence Interval
Total	108	112	99	88.4%	81, 93.7
Fixed Dose	58	60	54	90%	79.5, 96.2
Variable Dose	50	52	45	86.5%	74.2, 94.4

## RESULTS Continued

Chart 3



## CONCLUSIONS

Urine samples from a known adherent population at BIMC were analyzed using the proprietary algorithm to assess percent adherence based on the standardized range of the model. Patients who reported the use of a fixed dose regimen were only slightly more likely to have urine concentrations within the reference ranges determined previously than patients taking variable dose regimens, who could modify the dose based on pain intensity (90% vs. 86.5%). Thus, the model performed comparably for both fixed and variable dosing patterns.

Although different criteria were used to assess adherence between the two populations, these data support a model by which quantitative urine drug testing can contribute more meaningfully to adherence monitoring, and that this model generalizes well. When combined with other clinical indicators of non-adherence (e.g., aberrant behaviors), its use should enhance the ability of clinicians to identify patients who are non-adherent with chronic opioid therapy.

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