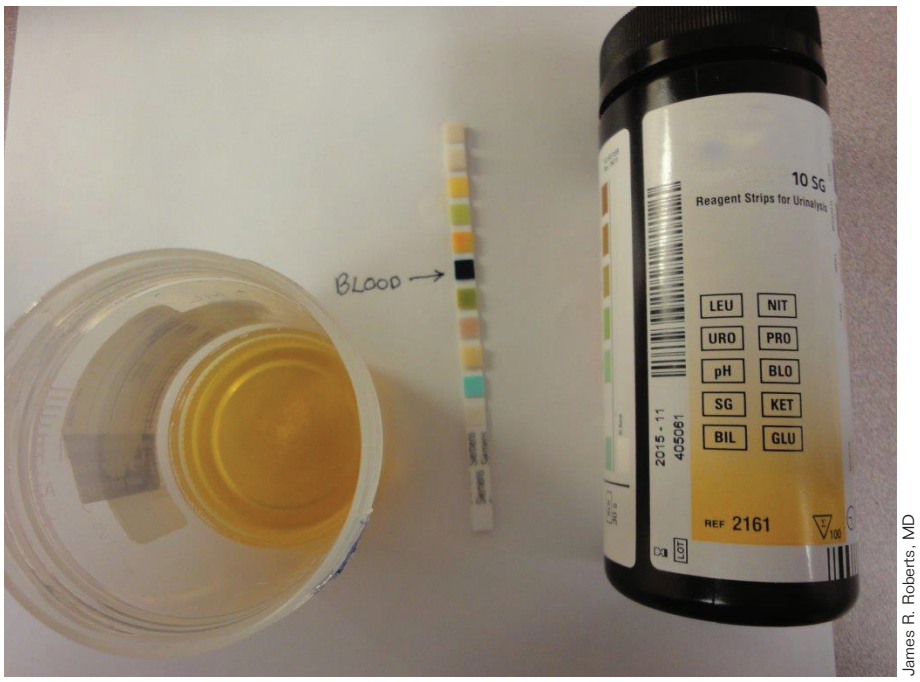
Urine Dipstick Testing: Everything You Need to Know

BY JAMES R. ROBERTS, MD

Think of all the times you order urinalysis each shift. It seems to be a straightforward test, and most physicians think they are well versed in the interpretation of the results: You give it a glance and make a decision. The dipstick analysis, the microscopic exam, and other information gleaned from a UA make their way into decision-making for a variety of diagnostic, therapeutic, and disposition issues. Like most things learned in detail many years ago, the interpretation of the UA should be revisited on a regular basis.

I find myself thinking I know everything about a certain test only to find that the guidelines have changed, technology has advanced, and previously held dogma is now relegated to the status of misconception. When one considers the complexity of the UA, it is obvious that this is not a simple test. The intricacies and subtleties are actually quite amazing. This month's column focuses on dipstick testing, and next month's will review urine microscopy.



James R. Roberts, MD

Clear urine with a dipstick strongly positive for blood usually means myoglobinuria. In such cases, the microscopic analysis would be negative for RBCs. Significant myoglobinuria can produce acute renal failure.

Urinalysis: A Comprehensive Review
Simerville J, Maxted WC, Pahira JJ
Am Fam Physician
2006;74(7):1096

The authors of this nifty review discuss the value of the standard UA for diagnosing many urinary tract conditions, including malignancy and metabolic issues. The review covers the correct method for performing urinalysis and highlights the importance and diagnostic value of a number of abnormal results found on the dipstick and with microscopy. Information gained for the UA is termed invaluable by these urologists from Georgetown University.

Specimen Collection: A midstream clean-catch technique is usually adequate for most men and women and in most ED situations. These authors say (and many would disagree) that the time-honored ritual of cleaning the external genitalia in women has little or no proven benefit, although it is commonly emphasized. Some reviews put the contamination rates as similar in specimens obtained with or without prior cleaning. (*Arch Intern Med* 2000;160[16]: 2537.) Urine should be refrigerated if it cannot be examined for more than two hours because delayed analysis can produce unreliable results.

Physical Properties: A variety of foods, medications, metabolic products, and infections can cause abnormal urine colors and odors. Normal urine is clear and light yellow in color. Concentrated urine produces a darker color, a common finding in the morning after overnight water restriction. Cloudy urine can be normal, usually caused by precipitated phosphate crystals in alkaline urine. Significant pyuria also can cause clouded urine.

Urine clarity is a good but not infallible guide to the presence or absence of UTI. (*Pediatrics* 2000; 106[5]:E60.) Many believe that odoriferous urine is a sign of infection, but it can simply represent a concentrated specimen or a particular diet. Urine that has prolonged bladder retention time can develop an ammonia-like odor. A fecal smell in the urine suggests a GI-bladder fistula. Certain foods such as asparagus or beets and a variety of medications can change the odor or color of urine. Myoglobin colors the urine brown, carrots can produce a deep yellow color, and pseudomonas infections, propofol, and amitriptyline may give a blue/green hue to the urine.

Dipstick Analysis: The accuracy of detecting microscopic hematuria, significant proteinuria, or urinary tract infection is a subject of much interest and practicality to emergency physicians. The urine dipstick has false-positive and false-negative results, and a list is presented in the table. It also should be noted that the commonly used urine dipstick has a finite lifespan, should be kept in a closed container, and should not be constantly exposed to air. Testing with outdated and improperly stored materials can lead to erroneous results. Dipstick testing is quite helpful, serving as a screening test for some conditions and a definitive test for others. Dipstick testing in complicated cases or serious disease must be correlated with microscopy and clinical parameters.

Urine Specific Gravity: Urine specific gravity (USG) generally correlates with the urine osmolality. The most useful information derived from the USG is insight into the patient's hydration status and the concentrating ability of kidneys. The latter function is disrupted in a variety of diseases.

The normal USG ranges from 1.003 to 1.030. USG less than 1.010 is suggestive of relative hydration, and values greater than 1.020 indicate relative dehydration. Pathologic conditions that increase the USG without regard to hydration included glycosuria and syndrome of inappropriate antidiuretic hormone secretion (SIADH). Osmolality is the more important parameter to measure in such cases. A decreased USG, also known as dilute urine, is associated with diuretic use, diabetes insipidus, adrenal insufficiency, aldosteronism, or a plethora of conditions causing impaired renal function.

It should be noted that the purpose of the kidney is to concentrate urine when needed. Many renal diseases alter this concentrating function and result in a fixed specific gravity — about 1.010, the specific gravity of the glomerular filtrate. This is known as isosthenuria, a condition seen, for example, in patients with renal dysfunction because of sickle cell disease.

Urinary pH: The urine pH generally reflects the serum pH, but the primary and normal function of the kidney is to acidify the urine. Normal serum pH is 7.4, but the normal urinary pH ranges from 4.5 to 8. Because of normal metabolic activity, the generally accepted normal pH of urine is about 5.5 to 6.5. The kidney cannot acidify the urine in renal tubular acidosis (RTA), so the urine can be alkaline while the patient's serum demonstrates a metabolic acidosis.

The urine pH can be related to diet. Acid urine can be the result of ingesting fruits (hence the use of cranberry juice) that acidify the urine. Diets high in citrate and in citrus fruits, legumes, and vegetables can cause alkaline urine. Meat eaters tend to have more acidic urine, and vegetarians tend to have alkaline urine. Alkaline urine in the presence of a documented UTI may suggest infection with a urea-splitting organism (such as proteus). Triple phosphate crystals (magnesium ammonium phosphate crystals) in alkaline urine can form

a staghorn calculus. Uric acid stones form in an acidic urine.

Hematuria: The strict definition of hematuria by the American Urological Association is the presence of three or more red cells per high-powered field in two of three urine samples. The urine dipstick is used to test for the peroxidase activity of erythrocytes, not for the actual presence of the physical RBC. Of course, myoglobin and hemoglobin produce a positive dipstick for hematuria because these substances also will catalyze this reaction; these are the end-products of hemolyzed RBCs or muscle breakdown. High doses of vitamin C will inhibit this process, and can invalidate the dipstick for this test. This also holds true for stool guaiac testing; vitamin C can produce a false-negative occult blood in stool. It has always been standard that a positive dipstick for blood in the absence of RBCs by microscopy is indicative of myoglobinuria or hemoglobinuria, not true hematuria.

The authors present a table listing 45 causes of hematuria; some rare ones, such as Fabry's disease, will likely escape the detection and knowledge of the emergency physician, but it is important to know that hematuria can be associated with malignant hypertension, numerous urinary tract cancers, infections, nephrolithiasis, nephritis (lupus) and vasculitis, tuberculosis, and a variety of drugs, including the obvious — heparin and warfarin.

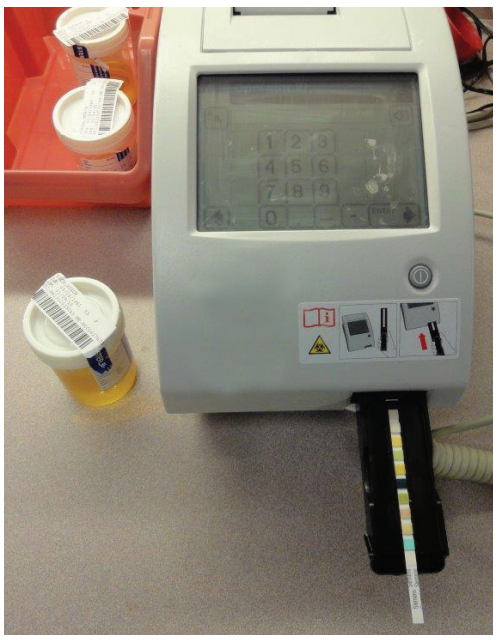
RBC casts are classic for acute glomerulonephritis. Hematuria also can be associated with TTP, renal vein thrombosis, sickle cell trait, or merely running a marathon. Contrary to popular belief, significant hematuria will not elevate the protein concentration to the required cutoff deemed positive, 3 plus or more on the dipstick. The authors note that up to 20 percent of patients with a gross hematuria have a urinary tract malignancy, so this condition requires a full workup. Hematuria, in the absence of proteinuria or RBC casts, suggests a pure urologic cause (stones/malignancy) for hematuria.

Proteinuria: Healthy kidneys limit the protein permeability of the glomerular capillaries, but diseased kidneys allow more protein to be filtered so proteinuria is a hallmark of a variety of renal diseases. Blood proteins are normally filtered and then reabsorbed by the proximal tubule cells. Urinary proteins include primarily albumin, but some serum globulins are detected. The actual definition of proteinuria is the excretion of more than 150 mg of protein per day. Patients with early renal disease may have microalbuminuria. Early diabetic nephropathy may not be detected by dipstick testing, so it is not a good screening test for this condition. The dipstick test is sensitive almost entirely to albumin; it will not detect low concentrations of globulins or the Bence-Jones proteins associated with multiple myeloma.

The dipstick is actually quite sensitive for proteinuria, and produces false-positive results by reacting to minor proteinuria that would not be considered clinically significant. Concentrated early morning urine may give the false impression of significant proteinuria. The authors state that the dipstick must be 3 plus or greater for protein to be considered significant. Interestingly, prolonged standing can produce proteinuria, termed orthostatic (postural) proteinuria. Iodinated radiocontrast agents and a highly alkaline urine may turn the dipstick falsely positive.

Glycosuria: Glucose is normally filtered by the glomerulus, but this substance is then almost completely absorbed in the proximal tubule. Glycosuria results when the amount of filtered glucose exceeds the kidney's ability to resorb, making glycosuria an abnormal finding. The blood glucose is usually at least 180 mg/dL to be detected by the dipstick.

Ketonuria: It is not normal to find ketones in the urine. Ketones are the product of fat metabolism that is commonly encountered in uncontrolled diabetes. Some ketonuria can occur normally in patients on a carbohydrate-free diet (high-protein weight loss diets) and occasionally with starvation or a prolonged fast.



James R. Roberts, MD

The eyeball analysis of dipsticks has been replaced with machine reading. This device reads the dipstick and transfers the results directly to an electronic medical record.

Nitrites: There is a difference between nitrates and nitrites. Although nitrates are excreted by the kidney, nitrites are not normally found in urine. The dipstick will identify this condition when bacteria reduce urinary nitrates to nitrites. One needs the presence of bacteria for the dipstick to register a positive nitrite.

A positive nitrite test usually means infection. It generally requires more than 10,000 bacteria per ml to turn the dipstick positive, making it a specific but not a very sensitive test. A negative nitrite test does not rule out a UTI, but a positive one strongly suggests infection. Infection with non-nitrate-reducing organisms will result in a negative nitrite test. If the diet is deficient in nitrates, the test may also be falsely negative in the presence of infection. The nitrite reagent on the dipstick is quite sensitive to environmental air, so this test is the one that is most affected when out-of-date dipsticks or those kept in an open container are used. Improperly stored dipsticks are the most common cause of a false-positive test for nitrites.

Leukocyte esterase: LE is an enzyme produced by neutrophils. It may signal pyuria associated with UTI. WBCs anywhere in the genitourinary tract, including the vaginal vault, will produce LE. The dipstick should be allowed to sit for at least 30 to 60 seconds before reading the LE test. LE is somewhat nonspecific, and will be positive in patients with chlamydia infections, urethritis, tuberculosis, bladder tumors, viral infections, nephrolithiasis, foreign bodies, and corticosteroid use.

Bilirubin and urobilinogen: Urine does not usually contain bilirubin. Any bilirubin found in the urine is conjugated bilirubin because unconjugated bilirubin cannot pass through the glomerulus. Biliary obstruction or liver disease will cause an elevated urine bilirubin. There can normally be small amounts of urobilinogen in the urine. Urobilinogen is the end-product of conjugated bilirubin after it passes through the bile duct and has been metabolized in the intestines. This urobilinogen is reabsorbed into the portal circulation and eventually filtered by the kidney. Patients with hemolysis or other types of liver disease will have an elevated urobilinogen level.

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Accuracy of Urinalysis for Disease Detection

Condition	Test	Results	Sensitivity (%)	Specificity (%)
Microscopic hematuria	Dipstick	≥1 + blood	91-100	65-99
Significant* proteinuria	Dipstick	≥3 + protein	96	87
Culture-confirmed UTI	Dipstick	■ Abnormal leukocyte esterase	72-97	41-86
		■ Abnormal nitrites	19-48	92-100
	Microscopy	■ >5 WBC/HPF	90-96	47-50
		■ >5 RBC/HPF	18-44	88-89
		■ Bacteria (any amount)	46-58	89-94

* Defined as 3 + or greater on dipstick.
Source: Adapted from *Am Fam Physician* 2006;74(7):1096.

Urine Testing

Continued from previous page

If the bile duct is obstructed, less bilirubin enters the intestine, and therefore less urobilinogen is detected in the urine.

Comment: This article is humbling, and makes the clinician yearn for the memory and recall prowess he had in medical school. One marvels at how the interpretation of the lowly UA dipstick has morphed into a very sophisticated science. The main take-home point from this discussion is that dipstick testing is not an exact science.

Physicians may think that they are well versed in the interpretation of a dipstick urinalysis, but a periodic review is helpful. It might not be a bad idea to carry this article in your briefcase because the information is difficult to find in general textbooks. I particularly liked the tables (45 causes of hematuria and 37 causes of proteinuria), which widen one's differential from just a kidney stone and cancer to such bizarre things such as IG nephropathy and Goodpasture's disease. No normal individual can possibly remember all these conditions during a busy shift.

Trace-positive dipsticks often confuse the clinician, and those done in the ED don't always match the lab tech's report. There is no totally agreed-upon standard about how to use the dipstick in the ED. Most clinicians use the dipstick to screen for problems, and eschew sending the UA to the lab for repeat testing or microscopy if the dipstick is totally negative. This seems reasonable. (*Clin Nephr* 1994;41[3]:167.) Positive findings may or may not prompt the lab to perform the same or additional studies. When serious pathology is suspected, however, one usually combines dipstick testing with microscopy and clinical information. Kidney stones, for example, can be associated with a 10 percent to 20 percent incidence of a negative dipstick for blood. Don't rule out a kidney stone solely on the basis of a negative dipstick. And hematuria is common with endocarditis and aortic dissection.

The dipstick for blood is probably the test result of greatest utility to the EP, but this is a very sensitive test that has a number of false-positives. The few RBCs that normally inhabit the urine (2–3) can give a trace reading.

The dipstick does not identify RBCs; it essentially detects the presence of RBC peroxidase activity, whether these cells are intact, or if there is merely free hemoglobin in the specimen. Even if the patient is on heparin or warfarin, gross hematuria has always prompted a consideration for malignancy. This is similar to finding occult blood in a stool sample in a patient on iron or aspirin. It may well be related to the drug, but you just can't say for sure. Dehydration and exercise will give a false-positive dipstick for true hematuria, and vitamin C (blocks peroxidase activity), captopril use, a pH less than 5.1, and proteinuria may produce a false-negative dipstick analysis for blood.

I frequently encounter trace to 1 plus protein via dipstick testing. It is rarely important in the ED. Trying to track down trace or 1 plus proteinuria is a useless task in the ED and probably in general practice. Unlike the dipstick that detects albumin, the sulfosalicylic acid test (SSA) detects all proteins in the urine. The SSA test would pick up a myeloma kidney (Bence-Jones light chain immunoglobulins).

With regard to specific gravity, one reason sickle cell patients often go into crisis when there is no good reason to be dehydrated is that they cannot concentrate their urine. Finding a USG of 1.010 in a patient with advanced sickle cell disease does not mean they are well hydrated. They may be quite dehydrated and unable to concentrate their urine. USG usually corresponds to osmolality, but large molecules in the urine, such as glucose or IV dye, can produce large changes in USG with relatively minimal changes in osmolality. It has been shown that there is no clear or consistent relationship between USG and osmolality so an osmometer should be used when osmolality determinations are important. (*Arch Dis Child* 2001;85 [2]:155.)

With regard to urinary pH (normal 4.5–8.0), there are many causes of alkaline urine, and not all patients with this finding have urea-splitting organisms. The kidney's task is to acidify urine, and normally a serum pH of 7.4 produces a urine pH of about 6.0. Interestingly, in the presence of urinary tract obstruction by a stone, the kidney loses its ability to secrete acid, and obstruction alone can produce alkaline urine. (*Pediatr Nephrol* 1988;2[1]:34.) Patients with a significant metabolic acidosis would be expected to produce an acidic urine, usually below 5.0. Higher pH would suggest RTA.

In my experience, finding a trace or 1 plus leukocyte esterase (LE) is commonly a falsely abnormal test. This is likely mostly because of contamination. Interestingly, nephrolithiasis alone, in the absence of infection, can produce a dipstick positive for LE. This may lead the clinician to suspect infection in the stone former when it is not present. With regard to the ability of the dipstick to diagnose UTI (confirmed by culture), the

Urine Dipstick Testing: Causes of False-Positive and False-Negative Results

Dipstick test	False-positive test	False-negative test
Bilirubin	Phenazopyridine (Pyridium)	Chlorpromazine (Thorazine), selenium
Blood[1]	Dehydration, exercise, hemoglobinuria, menstrual blood, myoglobinuria, semen in urine, highly alkaline urine, oxidizing agents uses to clean perineum	Captopril (Capoten), elevated specific gravity, pH <5.1, proteinuria, vitamin C, dipstick exposed to air
Glucose	Ketones, levodopa (Larodopa), dipstick exposed to air	Elevated specific gravity, uric acid, vitamin C
Ketones	Acidic urine, elevated specific gravity, some drug metabolites (e.g., levodopa)	Delay in examination of urine
Leukocyte esterase[3]	Contamination,[2] nephrolithiasis	Elevated specific gravity, glycosuria, ketonuria, proteinuria, cephalexin (Keflex), nitrofurantoin (Furadantin), tetracycline, gentamicin, vitamin C
Nitrites	Contamination, exposure of dipstick to air	Elevated specific gravity, elevated urobilinogen levels, nitrate reductase-negative bacteria, pH <6.0, vitamin C
Protein[4]	Alkaline or concentrated urine, quaternary ammonia compounds, iodinated radiocontrast agents	Acidic or dilute urine, primary protein is not albumin, such as Bence-Jones protein
Specific[5] gravity	Dextran solutions, IV radiopaque dyes, proteinuria	Alkaline urine
Urobilinogen	Elevated nitrate levels, phenazopyridine	

1. Test depends on peroxidase activity of RBC. Tests will be positive with intact or lysed cells. This test is very sensitive and may be positive in normal urine (1-2 RBC/HPF).
2. Especially vaginal contamination.
3. Sterile pyuria seen with interstitual nephritis, TB, and nephrolithiasis.
4. Not clinically significant unless 3 + or greater. Detects mainly albumin and requires protein excretions of 300-500 mg/day.
5. Accurate analysis for osmolality requires osmometer.

Adapted from *Am Fam Physician* 2006;74(7):1096.

specificity for a positive LE test can be as low as 41 percent.

Many organisms are capable of converting nitrates and nitrites, but non-nitrate-reducing organisms also can cause false-negative nitrite results. Of course, patients who consume a low-nitrate diet will not have the nitrate substrate for the bacteria to convert.

The nitrite test is much more sensitive for infection than the LE, although it takes a while for the bacteria to reduct the nitrates to nitrites. The urine must remain in the bladder for some time, and I could not determine the exact specifics. Importantly, if your dipsticks are scattered around the ED lab in an open container for more than two weeks, about three-quarters of them will give a false-positive result for nitrites. Perhaps the lab is better at protecting dipsticks than the ED, but I rarely see the top put back on the container in my ED's stat lab. Everyone has difficulty with quality control for dipstick testing in the ED. We all now use machines to read the dipstick rather than relying on a nurse's eyeball, and a printout has replaced the pen. Nonetheless, our hospital lab often disagrees with the ED reading for leukocyte esterase and the degree of hematuria.

The heterogeneity of dipstick accuracy for UTI is subject to ongoing discussion. One exhaustive meta-analysis concluded that the urine dipstick test alone seems to be useful in all populations to exclude infection if nitrites and leukocyte esterase are negative. (*BMC Urol* 2004;4:4.) The sensitivity for each test alone is quite variable, from 60 to 88 percent, but a negative result is sufficiently predictive enough to exclude disease. Dipstick results should be combined with clinical acumen, but send a urine culture when in doubt.

Like most things in medicine, the dipstick urinalysis is not as straightforward as one would like. It is clearly not foolproof or a gold standard for many things. A plethora of conditions produce false-positive or false-negative results. It can serve as a useful guide to the emergency physician as a screening test or as a diagnostic test, but there are times when the dipstick must be correlated with other testing and clinical information. **EMN**

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Learning Objectives for This Month's CME Activity: After participating in this CME activity, readers should be better able to interpret dipstick urinalysis results to aid decision-making for a variety of diagnostic, therapeutic, and disposition issues.

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In Brief

Trainee Consultants Leaving Scottish ED

Consultant trainees at the Royal College of Physicians and Surgeons of Glasgow (RCPG) in Scotland are leaving to enter other specialties after witnessing the pressure put on their certified counterparts. The issue, according to the president of RCPG, needs to be addressed as a matter of urgency, according to the Scottish newspaper, *The National*.(25 March 2015; http://bit.ly/1xirJzI.)

Consultants are already overextended without adding the component of properly and thoroughly training their successors. That leads trainees, after seeing consultants constantly struggling, to decide it's not for them. This decision ultimately puts a damper on trainee retention.

In another effort to retain trainees, the RCPG has backed the Royal College of Emergency Medicine (RCEM) of Scotland in its campaign, Step, to help improve the quality and safety of emergency care in hospitals across Scotland. "We have continued to drive increased recruitment within our emergency departments," said Shona Robison, Scotland's Secretary of Health.

"Since September 2006, the number of emergency medicine consultants has risen from 75.8 whole-time equivalent staff to 205 — an increase of 170.6 per cent — and we are committed to working with the RCEM on this issue."

No Benefit of Nicotine Patches After Six Months

Patients do not receive any added benefit of wearing nicotine patches beyond 24 weeks of treatment, according to a study published in *JAMA*. (http://bit.ly/1JHsl7G.)

Researchers compared the standard eight-week treatment, an extended 24-week treatment, and a 52-week maintenance treatment for promoting tobacco abstinence. More than 500 treatment-seeking smokers participated in a randomized clinical trial that took place from June 2009 through April 2014 at two universities.

Twenty-one percent of participants in the standard treatment group were abstinent at the end of 24 weeks, compared with 27 percent of participants in the extended and maintenance treatment groups. Participants in the extended and maintenance treatment groups reported significantly greater abstinence rates at 24 weeks, compared with participants in the standard treatment group who had a longer duration of abstinence until relapse, and reported more abstinent days.

At 52 weeks, participants in the maintenance treatment group did not report significantly greater abstinence rates, compared with participants in the standard and extended treatment groups.

Feds Speed Plans for Value-Based Payments

The U.S. Department of Health and Human Services said it would fundamentally reform how it pays providers for treating Medicare patients in the coming years.

"Today, for the first time, we are setting clear goals — and establishing a clear timeline — for moving from volume to value in Medicare payments. We will use benchmarks and metrics to measure our progress; and hold ourselves accountable for reaching our goals," said HHS Secretary Sylvia Mathews Burwell in an official announcement.

Those goals are for 30 percent of all Medicare provider payments to be in alternative payment models that are tied to how well providers care for their patients, instead of how much care they provide and to do it by 2016 and for virtually all Medicare fee-for-service payments to be tied to quality and value (at least 85 percent in 2016 and 90 percent in 2018).

HHS announced the creation of a Health Care Payment Learning & Action Network to facilitate the public-private sector partnership, and they plan to hold the first meeting in March. The announcement marks the Obama administration's biggest effort yet to shape how physicians are compensated across the health care system, according to a *Washington Post* article. Read more: http://wapo.st/1thNhuc & http://1.usa.gov/1zk2YUx.