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BRIEF REPORT

# Potassium and phosphorus repletion in hospitalized patients: implications for clinical practice and the potential use of healthcare information technology to improve prescribing and patient safety*

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***Key words:*** **Healthcare information – Phosphate – Phosphorus – Potassium – Prescribing – Safety**

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## ABSTRACT

*Objectives:* Evaluate potassium and phosphorus repletion in hospitalized patients. Assess the potential role for use of various methods, including healthcare information technology, to improve prescribing and patient safety.

*Research design and methods:* Inpatient medication profiles were screened to identify orders for potassium and phosphorus replacement products. Electronic laboratory and medical records were used to evaluate efficacy and safety. Eligibility for oral therapy was defined by the presence of other scheduled oral medications on the medication profile. Appropriateness of prescribing was based on adherence to the hospital guidelines for repletion.

*Results:* Overall, 134 orders for potassium in 92 patients and 36 orders for phosphorus in 27 patients were evaluated over a 3-week data collection period. Intravenous (IV) potassium was prescribed in 73% of replacement episodes (46% as single doses and 54% within large volume IV fluids), with 85% for normokalemia or mild-to-moderate cases of hypokalemia. Phosphorus orders involved single doses of IV potassium phosphate (mean 13.1 mmol) in 75% of cases. Approximately 85% of doses were for mild or moderate hypophosphatemia. Eligibility for oral therapy was evident in 74% of normokalemic or mild hypokalemic cases receiving IV potassium products and in 33% of cases receiving IV phosphorus replacement. Six cases of mild hyperkalemia were observed. No hyperphosphatemia was documented.

Study limitations include use of a retrospective design, inability to discern whether some electrolyte doses were given with a preventative intent, potential overestimation of the number of patients eligible for oral repletion, and lack of data on the accessibility of the laboratory serum concentrations or the awareness of serum values to the prescribers.

*Conclusions:* Intravenous potassium and phosphate products are commonly prescribed for mild or moderate cases of hypokalemia or hypophosphatemia. Many patients met eligibility for oral therapy. Efforts to enhance prescriber education and implement computerized prescribing and decision support systems have the potential to improve prescribing and reduce possibilities of adverse drug events and medication errors related to potassium and phosphate administration.

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## Introduction

Within the human body potassium is the most abundant cation, while phosphorus is the sixth most abundant element[1–3]. Both play vital roles in numerous important physiologic processes. Hypokalemia, typically defined as a serum potassium concentration below 3.5 mmol/L, is an electrolyte disturbance that is commonly encountered in hospitalized patients. A retrospective analysis of approximately 58 000 hospitalized patients over a 3-year period revealed that 20% of patients had a serum potassium concentration less that 3.5 mmol/l during their hospital admission[4]. Significant reductions in serum potassium concentrations may predispose patients to serious adverse effects, such as disturbances in cardiac conduction and muscle function.

Plasma phosphorus concentrations, typically measuring the 30% present as circulating inorganic forms, generally range from 2.8 to 4.5 mg/dl in adult patients[5]. Hypophosphatemia, routinely defined as a plasma phosphorus concentration of less than 2.7 mg/dl, is an electrolyte disorder that is frequently encountered in hospitalized patients. Moderate hypophosphatemia (serum phosphorus concentration less than 2 mg/dl) has been reported in up to 2.15% of hospitalized patients, while severe hypophosphatemia (less than 1.0–1.5 mg/dl) has been reported to occur less frequently (0.1–0.24%)[6–10]. Higher incidences of hypophosphatemia have been reported in up to 28% of select patient populations within the hospital setting, such as those patients residing in intensive care units (ICUs)[7,10]. Given that phosphorus is present in relatively low circulating amounts in the bloodstream, large decreases in serum values may have detrimental physiologic effects on cardiac, respiratory, and muscle function. Despite the potential adverse effects of hypophosphatemia, acute phosphate replacement may not be necessary in all hospitalized patients, as most with mild-to-moderate hypophosphatemia are often asymptomatic. Likewise, hypophosphatemia may be transient and is often rapidly reversible if common causes such as respiratory alkalosis, primary hyperparathyroidism, or diabetic ketoacidosis are corrected[5]. Patients with true depletion of phosphate stores, or those with severe hypophosphatemia are candidates for phosphate repletion, possible utilizing intravenous therapy if necessary[5–7].

Appropriate prescribing of both potassium and phosphorus replacement products is essential, as each has been associated with the development of serious adverse drug events in hospitalized patients. Electrolytes, including potassium, have been implicated in up to 3.6% of preventable adverse events or medication errors in hospitalized patients[11,12]. Injectable potassium and phosphate products, particularly in concentrated forms, are considered among the top five 'high-alert' medications identified by the Institute for Safe Medication Practices[13]. The use of IV potassium and phosphate replacement products may also result in increased nursing time for administration, as potential adverse effects limit the quantity dispensed per IV dose as well as the rate of IV infusion. However, the use of intravenous potassium and phosphate products do play a role in patients requiring rapid replacement due to depletion of body stores, in those experiencing clinical manifestations of deficiency, or in those patients who do not have oral access. Patients with severe hypophosphatemia in whom intravenous therapy would be appropriate include those experiencing mental status changes, seizures, hemolysis, or rhabdomyolysis[2]. Likewise, severely hypokalemic patients experiencing cardiac instability or arrhythmias, or those lacking oral access may require intravenous repletion. In most other cases the oral route of administration is typically sufficient[14].

Despite the critical safety issues involved with potassium and phosphate repletion, prescribing practices at the institutional level are not well studied. Appropriate use of potassium and phosphate replacement products is necessary for adequate repletion and avoidance of adverse events that may result from inappropriate dosing or product selection, yet few studies have evaluated the choice of formulation, or safety and efficacy of replacement in hospitalized patients. The main objectives of this retrospective study were to characterize the use of potassium and phosphate replacement products and evaluate the efficacy, safety, and appropriateness of prescribing in hospitalized adult patients, including patient eligibility for oral replacement when IV repletion was prescribed. In addition, generation of data to be directly utilized to delineate the effects of implementing healthcare information technology on prescribing and patient safety of potassium and phosphate replacement products at our institution was the final objective.

## Patients and methods

Adult inpatient medication profiles at the University of Colorado Hospital, a 400-bed academic medical center, were screened during a 3-week period in April/May of 2003 for the presence of potassium and phosphate replacement products. Patients were included if they were admitted to either a medical or surgical floor, or a medical or surgical intensive care unit (ICU), and received at least one oral or IV dose of a formulary potassium or phosphorus replacement agent during the study time period. It was not possible to accurately obtain concentrations for potassium


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or phosphate administered via parenteral or enteral nutrition, so these routes of administration were not included in this evaluation. Each patient medication profile and drug order evaluated provided a description of the product ordered, including drug formulation, dose, route, frequency and rate of administration, the day and time of the initial order, and the stop date for administration, if applicable. For IV potassium products, large volume replacement was considered to be any order for repletion that was administered in greater than 500 ml of a compatible fluid. Electronic laboratory and medical records were then used to obtain the patient's medical history and to evaluate the efficacy of each episode of potassium and phosphate repletion. Efficacy was assessed by comparing serum potassium or phosphate concentrations available immediately prior to the replacement episode with the next available serum concentration following administration. Eligibility for oral therapy was defined by the presence of at least one scheduled oral medication on the patient's drug profile at the time of the initial potassium replacement order, including those administered via orogastric or nasogastric tubes.

Appropriateness of therapy was based on adherence to hospital potassium and phosphorus replacement guidelines (Table 1), and assessment of potential for use of an oral product when IV replacement was ordered. Safety was assessed by evaluating documentation of an adverse event related to potassium or phosphorus replacement in the patient's medical record, or by documenting a medication order for sodium polystyrene sulfonate, insulin, sodium bicarbonate, or an inhaled $\beta_2$-adrenergic agonist written for immediately following laboratory evidence of hyperkalemia. Data analysis using descriptive statistics was performed. The study was approved by the Colorado Multiple Institutional Review Board.

## Results

A total of 134 orders for potassium replacement products in 92 patients, and 36 orders for phosphorus replacement products in 27 patients, were evaluated. The population was a mixture of patients located on both medical and surgical floors and ICUs (Table 2.). The mean serum concentrations upon admission were 3.8 mmol/L (range 2.2–6.0 mmol/L) for potassium and 3.1 mg/dl (range 1.9–3.9 mg/dl) for phosphate. Evaluation of potassium and phosphorus replacement stratified using the serum concentrations outlined in the hospital replacement guidelines revealed that most orders were for patients with normal serum potassium values (46%) or mild hypokalemia (28%). Likewise, the majority of orders for phosphate replacement products were in patients with mild-to-moderate hypophosphatemia (Table 3).

The characteristics of replacement episodes of potassium and phosphorous are presented in Tables 4 and 5, respectively. In general, 73% of potassium orders were for IV replacement products, and 53% of all orders were for single replacement doses. The mean dose per potassium replacement order was 25 mEq (range 10–80 mEq), and quantification of the average total daily potassium replacement considering all prescribed doses was 36 mEq/day (range 10–80 mEq/day). Orders for IV potassium replacement were almost equally distributed between large- and small-volume formulations, and 49% of all IV replacement orders were written as single doses. Fifty-eight percent ($n$ = 41) of IV potassium doses were given in a non-ICU setting. Twenty-seven percent of orders were written for oral replacement products, 64% of those were for single doses, and 94% were for tablet formulations of potassium. Patients with normal serum potassium concentrations

***Table 1.*** *Hospital guidelines for phosphate and potassium replacement*

| Serum phosphorus | Recommendations for repletion |
|---|---|
| Normal (2.7–4.5 mg/dl) | |
| Mild hypophosphatemia (2.1–2.4 mg/dl) | No treatment or sodium potassium phosphate (K-phos neutral) 500 mg PO TID |
| Moderate hypophosphatemia (1–2 mg/dl) | Sodium phosphate 5–10 mmol (0.1 mmol/kg) IV over 4–6 h |
| Severe hypophosphatemia (< 1 mg/dl) | Sodium phosphate 10–20 mmol (0.2 mmol/kg) IV over 4–6 h |
| **Serum potassium** | **Recommendations for repletion** |
| Normal (3.7–5.0 mEq/L) | |
| Mild hypokalemia (3.1–3.4 mEq/L) | KCl 40 mEq PO × 1<br>*or*<br>KCl 10 mEq IV over 1 h × 3–4 doses |
| Moderate hypokalemia (2.6–3.0 mEq/L) | KCl 20 mEq PO every 2 h × 3 doses<br>*or*<br>KCl 10 mEq IV over 1 h × 4 doses; recheck and repeat × 2–4 doses if indicated |
| Severe hypokalemia (< 2.5 mEq/L) | KCl 40 mEq IV over 2–4 h; recheck and repeat<br>KCl 40 mEq IV over 4 h if indicated |

KCl = potassium chloride; mEq = milliequivalents; PO = oral; IV = intravenous

**Table 2.** *Patient demographics*

| | Potassium | Phosphate |
|---|---|---|
| Male/female (*n*) | 41/51 | 11/16 |
| Mean age (years), range | 55 (20–89) | 56 (23–89) |
| Location (*n*) | | |
| Medical floor | 29 | 10 |
| Surgical floor | 34 | 3 |
| Medical ICU | 11 | 9 |
| Surgical ICU | 18 | 5 |

**Table 3.** *Potassium and phosphorus replacement orders stratified by serum concentration*

| Serum potassium concentration (*n* = 134) | Orders, *n* (%) |
|---|---|
| Normal (> 3.5 mEq/L) | 61 (46) |
| Mild hypokalemia (3.1–3.4 mEq/L) | 37 (28) |
| Moderate hypokalemia (2.6–3.0 mEq/L) | 19 (14) |
| Severe hypokalemia (< 2.5 mEq/L) | 1 (1) |
| Hyperkalemia (> 5.0 mEq/L) | 1 (1) |
| No baseline serum value | 15 (10) |
| Serum phosphorus concentration (*n* = 36) | |
| Normal (2.7–4.5 mg/dl) | 4 (11) |
| Mild hypophosphatemia (2.1–2.4 mg/dl) | 14 (39) |
| Moderate hypophosphatemia (1–2 mg/dl) | 17 (47) |
| Severe hypophosphatemia (< 1 mg/dl) | 1 (3) |

were the largest population receiving either oral or IV replacement. Approximately 83% of prescribed doses were not consistent with the replacement guidelines based on serum potassium concentration. Additionally, both oral and IV potassium replacement products were ordered for patients with hyperkalemia (*n* = 1), or no available baseline serum potassium value (*n* = 15). Five patients had lidocaine added to their IV potassium replacement fluid following the initial administration of their replacement dose, indicating possible development of injection site pain or phlebitis. Sixty-nine percent of patients receiving IV potassium repletion were deemed eligible for oral replacement therapy. The majority (85%) of these patients had serum potassium concentrations that were classified as either normal, mild or moderate in severity.

Regarding adverse outcomes, six patients developed mild hyperkalemia following their initial potassium replacement order, with serum potassium values ranging from 5.1 to 5.7 mmol/L. No patient received any specific medication treatment for hyperkalemia, and no identifiable adverse events related to these episodes were documented in the medical record.

Seventy-five percent of phosphate replacement episodes involved single doses of intravenous potassium

**Table 4.** *Characteristics of potassium replacement orders in hospitalized adults (*n = *134 orders)*

| | |
|---|---|
| Dose per order* (mEq)(mean, range) | 25 (10–80) |
| Total $K^+$ replacement (mEq/day) (mean, range) | 36 (10–80) |
| Single doses (*n*) | 71 |
| IV replacement orders* (*n*) | 98 |
| Single dose (*n*) | 48 |
| Single dose small volume (*n*) | 45 |
| Small volume (*n*) | 45 |
| Large volume (*n*) | 53 |
| Normokalemia (*n*) | 43 |
| Mild hypokalemia (*n*) | 27 |
| Moderate hypokalemia (*n*) | 13 |
| Severe hypokalemia (*n*) | 0 |
| Hyperkalemia (*n*) | 1 |
| No baseline serum potassium value (*n*) | 14 |
| Oral replacement orders* (*n*) | 36 |
| Tablet/liquid (*n*) | 34/2 |
| Single dose (*n*) | 23 |
| Normokalemia (*n*) | 18 |
| Mild hypokalemia (*n*) | 10 |
| Moderate hypokalemia (*n*) | 6 |
| Severe hypokalemia (*n*) | 1 |
| Hyperkalemia (*n*) | 0 |
| No baseline serum potassium value (*n*) | 1 |

*All orders were for potassium chloride; mEq = milliequivalents; $K^+$ = potassium

**Table 5.** *Characteristics of phosphorus replacement in hospitalized adults (*n = *36 orders)*

| | |
|---|---|
| Dose per order (mmol)(mean, range) | 13.1 (4–20) |
| Intravenous replacement orders (*n*) | 27 |
| Single dose (*n*) | 27 |
| Mild hypophosphatemia (2.1–2.4 mg/dl) | 11 |
| Moderate hypophosphatemia (1–2 mg/dl) | 12 |
| Severe hypophosphatemia (< 1 mg/dl) | 1 |
| Normal serum phosphorus | 3 |
| Potassium phosphate (*n*) | 27 |
| Oral replacement orders (*n*) | 9 |
| Single dose (*n*) | 3 |
| Mild hypophosphatemia (2.1–2.4 mg/dl) | 3 |
| Moderate hypophosphatemia (1–2 mg/dl) | 5 |
| Severe hypophosphatemia (< 1 mg/dl) | 0 |
| Normal serum phosphorus (2.7–4.5 mg/dl) | 1 |

mmol = millimoles

phosphate (mean 13.1 mmol). Forty-one percent of intravenous use was for mild cases of hypophosphatemia (2.1–2.4 mg/dl), and 44% for moderate (1–2 mg/dl). Normalization of phosphorus upon initial repeat lab assessment was 61%. Thirty-three percent of mild cases receiving intravenous replacement were eligible for oral therapy, and 85% were eligible for alternate use of sodium phosphate instead of potassium


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phosphate based on average potassium and sodium values of 4.1 mEq/L and 139 mmol/L. No episodes of hyperphosphatemia were documented.

## Discussion

Overall, hypokalemia and hypophosphatemia were documented in 54% ($n$ = 88) and 89% ($n$ = 32) of study subjects receiving a potassium or phosphate replacement product. Use of IV preparations was observed in 73% of potassium orders ($n$ = 98) and 75% ($n$ = 27) of phosphate orders despite the presence of mostly mild-to-moderate cases of hypokalemia and hypophosphatemia. Most orders were for single replacement doses of these IV products, which were often prescribed for patients with normal serum values. Likewise, patients who received IV potassium or phosphate preparations appeared to have the ability to receive medications orally in 69% and 33% of cases, respectively. Potassium, in many instances, was an additive to larger IV fluid solutions the patient was receiving, and may therefore be overlooked as a source of potassium intake. For patients with hypophosphatemia, IV potassium phosphate was preferentially used for repletion, despite sodium phosphate being the preferred IV phosphate replacement agent at our institution. Another finding was that only 17% of initial potassium orders and 31% of initial phosphate orders followed dosing recommended by the available hospital replacement guidelines. The results of this study highlight several important aspects of determining the quantity and route of administration of electrolyte preparations in the hospital setting.

The results of this study also demonstrate the high frequency with which potassium replacement is implemented in hospitalized patients, as over 100 orders for potassium replacement products were identified within a 3-week period. This equates to over 2000 potential orders for potassium replacement products on an annual basis. In comparison, a study conducted in a large tertiary-care hospital in Israel identified 636 inpatients with serum potassium concentrations below 3.0 mEq/L over a 6-month period[15]. The rate of reported hypokalemia was slightly lower than reported in this study, however we included a large percentage of patients with mild hypokalemia, whereas the previous study did not. Mild hypokalemia, typically defined as a serum potassium concentration between 3.0 and 3.4 mmol/L, is the most frequently reported disturbance in potassium encountered in hospitalized patients. A retrospective study evaluating over 12 000 instances of hypokalemia in hospitalized patients revealed that 75% had serum potassium values between 3.0 and 3.4 mmol/L[4]. The patients included in the present study were also distributed among several different patient-care areas, including medical and surgical floors and ICUs. This demonstrates that hypokalemia is a common problem regardless of the hospital area of practice or patient type and is reflected in our findings as well. As mentioned previously, studies evaluating hospitalized patients demonstrate that mild-to-moderate hypophosphatemia constitutes the majority of patients identified[7–9]. Again, this is consistent with our findings.

Guidelines for the treatment of hypokalemia recommend the use of oral agents at a moderate dose, typically between 40 and 200 mmol per day, over a period of days to weeks in order to ensure full repletion of potassium stores[16]. As discussed earlier, IV phosphate and potassium preparations are typically recommended for treatment of severe cases or in symptomatic patients[5–7,14,17–20]. Patients with severe hypokalemia or hypophosphatemia represented the minority of cases observed in this study. The greater use of IV agents may be a reflection of the perception that IV therapy is needed for prompt replacement to avoid adverse outcomes, that IV products have superior efficacy over oral products, or that it is simply easier to administer these products based on the availability of IV access. Few studies have evaluated the method of phosphate repletion used to correct hypophosphatemia. In one series, six of 22 patients with severe hypophosphatemia were treated with oral replacement therapy[7]. Most other published data report single or repeated dosing of IV phosphate preparations for correction of severe hypophosphatemia, mainly in critically ill patients[10,21–28]. These data reinforce the suggestion that IV phosphate preparations should be reserved for severe cases in hospitalized patients.

The prescribing of these preparations in patients with normal serum values may reflect the preventative use in patients receiving certain medications, such as diuretics, or the continuation of potassium or phosphate regimens prescribed on a outpatient basis. Given that a majority of patients receiving IV potassium and phosphate were potentially eligible for oral therapy, this may also reflect a lack of prescriber knowledge in relation to the identification of appropriate clinical scenarios where use of an IV product may be warranted.

Studies have evaluated efforts to improve appropriate use of potassium and phosphate in the hospital setting. Those efforts have focused on the distribution of prescribing guidelines, linkage of pharmacy and laboratory data on hospital computer systems, and implementation of computerized physician order entry (CPOE) and computerized clinical decision support (CDSS) systems. A study by Acker and colleagues evaluated the effect of providing guidelines for managing hyperkalemia directly to the physician provider at the time of laboratory identification of an elevated serum potassium value[29]. No improvement in

managing hyperkalemia was evident for those physicians who received the guidelines versus those who did not. In fact, those who did not receive the guidelines fulfilled the criteria for appropriate treatment of hyperkalemia more often than those who received the guidelines (50 vs. 30%; $p < 0.05$). Data from a meta-analysis evaluating provider compliance with practice guidelines for 143 medical and surgical procedures revealed that only 54% of provider's practices were consistent with published guideline recommendations[30]. Therefore, poor compliance to guidelines in various aspects of healthcare appears to be a widespread problem and may represent a reason why we observed poor compliance with our institutional guidelines.

Other methods that may be used to improve adherence to institutional guidelines include education of providers. Several educational modalities designed to educate providers and enhance appropriate treatment or use of a wide variety of medications have been studied[31–36]. Examples of educational interventions from these studies include provision of educational memoranda, direct contact and education of the provider at the time of prescribing, formal presentations or lectures, letter mailings, and medical chart reminders. While in most instances there were positive benefits derived from provider education, these educational efforts did not totally eliminate inappropriate prescribing or result in 100% guideline compliance.

Recent advances in enhancing patient safety, drug efficacy and adherence to prescribing guidelines involve the use of health information technology (HIT). Such systems include linkage of laboratory and pharmacy computer systems to provide real-time computerized alerts, and CPOE and CDSS systems. Published studies suggest that these systems may improve the use of various medications, including electrolytes[37–40]. In one study computerized alerts resulted in a 28% reduction in the number of hypokalemic episodes that were never normalized (17.5 vs. 12.5%, $p = 0.02$)[15]. Prescriber access to current laboratory data indicating normal or elevated potassium concentrations may not deter inappropriate prescribing of potassium replacement products, as a trial which reviewed over 30 000 prescriptions for potassium replacement products revealed that 1.5% of prescriptions were written for patients with serum potassium concentrations greater than 5.3 mmol/l[37]. To our knowledge no studies have evaluated the use of these systems for phosphate replacement in hospitalized patients.

Variable effects of CPOE on several aspects of patient safety are evident, and recent concerns have been expressed that CPOE systems may actually increase the frequency of certain types of medication errors[38–41]. Most CDSS studies focus on dosing and reducing complications related to specific medications, such as aminoglycoside antibiotics, warfarin, and theophylline. Results of studies focusing on antibiotic dosing have revealed lower rates of toxic serum concentrations, improved susceptibility of institution specific pathogens, and decreases in adverse drug events[39]. More studies evaluating the use of HIT in the setting of electrolyte replacement in hospitalized are warranted.

Despite these findings there are several limitations to this study. The retrospective design limited our ability to gather patient specific data regarding past medical history and complications of potassium or phosphate therapy. The use of medication profiles was adequate to identify patients receiving potassium replacement products; however, without evaluating the actual patient medication administration record, it could not be determined that all doses were actually administered. We were also unable to discern whether some doses given in the current study were prescribed with preventative intent. Given that some patients were receiving diuretics, this may have been the case in some instances. Eligibility for oral administration of potassium repletion may have been overestimated, as utilizing the presence of another oral scheduled medication on the patient medication profile as an indicator of eligibility for oral therapy may have excluded the possibility of other reasons for use of an IV over an oral preparation. We were unable to collect data on the accessibility of the laboratory serum potassium concentrations or the awareness of serum values to the prescribers. However, given that this study was conducted in an academic medical center, it can be speculated that laboratory values are evaluated on a daily basis by the patient's providers.

## Conclusion

The results of this study revealed that IV potassium and phosphate products were used for the majority of replacement episodes identified, despite the presence of mostly mild-to-moderate cases of hypokalemia and hypophosphatemia. Most patients were deemed eligible for oral replacement therapy, and poor compliance with the institution potassium and phosphate replacement guidelines was also apparent. Methods to improve the appropriate use of potassium and phosphate products and enhance patient safety may include targeting provider education and implementing computer-assisted modalities, such as CPOE and CDSSs. While the computerized methods have not been extensively studied in the setting of electrolyte replacement, several aspects of these systems may lend themselves well to use in this setting. More studies evaluating the effects of healthcare information technology on appropriate prescribing of electrolyte replacements are needed.


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