

# Linking Laboratory and Pharmacy

## Opportunities for Reducing Errors and Improving Care

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A myriad of errors and lost improvement opportunities result from failure of clinical laboratory and pharmacy information systems to effectively communicate. Pharmacotherapy could benefit from enhanced laboratory-pharmacy linkage with respect to (1) drug choice (laboratory-based indications and contraindications), (2) drug dosing (renal or hepatic, blood level-guided adjustments), (3) laboratory monitoring (laboratory signals of toxicity, baseline and ongoing monitoring), (4) laboratory result interpretation (drug interfering with test), and (5) broader quality improvement (surveillance for unrecognized toxicity, monitoring clinician response delays). Linkages can be retrospective or real-time. Many organizations could benefit now by linking existing pharmacy and laboratory data. Greater improvement is possible through implementation of electronic order entry with real-time decision support incorporating linked laboratory and pharmacy data. While many guidelines, admonitions, and rules exist regarding drugs and the laboratory, substantial new knowledge and evidence in this area are needed. Focusing on these unmet needs and accompanying logistical challenges is a priority.

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A physician prescribes potassium supplementation for a patient who is hyperkalemic, fails to adjust the dose of gentamicin in a patient with impaired renal function, continues a theophylline infusion in a patient who has toxic theophylline levels, continues an antibiotic for a patient whose blood cultures show an organism resistant to that drug, or fails to perform recommended monitoring of liver or muscle enzyme tests in patients taking

troglitazone or cerivastatin sodium. These are examples of errors that have occurred commonly, yet could have been prevented if laboratory and pharmacy information systems communicated more effectively.<sup>1-7</sup>

Drug errors related to laboratory issues commonly injure patients, both inside and outside the hospital. One study found that adverse drug events occurred in 6.5 of 100 admissions; 28% of these adverse drug events were judged preventable. Errors were most often due to drug dosing and selection problems related to laboratory parameters.<sup>8</sup> Using computerized screening, Hulse et al<sup>9</sup> found that 5% of 13 727 patients had potential drug problems, with drug-laboratory issues representing the leading reason (44.9% of the positive screens). In another inpatient study of more than 2100 pharmacist-detected medication errors, the leading type of error identified (13.9% of all errors) was excessive dosing for patients with impaired renal and hepatic function.<sup>10</sup> Adverse drug events also occur frequently in

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nursing homes, where an even greater proportion are preventable.<sup>11</sup> In this setting, insufficient laboratory monitoring, especially for anticoagulation therapy, is a leading cause of error.<sup>11</sup> Although fewer data are available for outpatients, medication-related problems are common outside the hospital, and deficiencies in monitoring are especially prominent.<sup>12</sup> One recent study found that 79% of adverse drug events detected by linking drugs with laboratory “signals” went routinely unrecognized.<sup>13</sup>

Laboratory information is critical to selecting and managing medications, yet the clinical laboratory and pharmacy are remarkably disconnected.<sup>1,13,14</sup> While the pharmacy is responsible for filling orders and dispensing medications, the laboratory monitors various effects of these administered chemicals. Despite this complementary relationship between the clinical laboratory and the pharmacy, these 2 departments, their personnel, their work processes, and particularly their information systems rarely communicate.<sup>14,15</sup> This is especially true in the outpatient setting, where the vast majority of drugs and tests are ordered.<sup>12</sup>

This disconnect even carries over to quality improvement efforts, which often fail to leverage laboratory and pharmacy data to reduce errors and improve care.<sup>16-19</sup> For example, at the laboratory end, recent symposia on improving the clinical use of laboratory information fail to even mention linkages with medications,<sup>20-23</sup> and an otherwise comprehensive pharmacist-edited book from the Institute for Safe Medication Practices on preventing medication errors barely touches on the subject of better connection to the laboratory.<sup>24</sup>

### LINKING LABORATORY AND PHARMACY: RATIONALE AND MODEL

Many medication errors could be prevented if laboratory and pharmacy information systems “talked with each other.”<sup>16,25</sup> However, frank errors are just the tip of the iceberg. Communication between these 2 systems, linked with appropriate knowledge-based rules, has broad potential to improve the quality of medical care.<sup>9,26-29</sup> With such linkages, drug toxicity can be more reliably prevented and more promptly

recognized and addressed when it does occur.

Linking tests and treatments can improve the utilization and quality of both laboratory testing and pharmacotherapy, as well as create opportunities for improved outcomes and learning. Such linkages can either be retrospective, linking downloaded laboratory and pharmacy files, or real-time via emerging intelligent order-entry systems. Although most hospitals and health systems do not currently have the capability for real-time linkage, virtually all could, but fail to, retrospectively tap into existing systems to link laboratory and pharmacy data, thereby missing improvement opportunities residing in existing data systems.

In this article, we describe 10 ways in which laboratory and pharmacy data can be related to improve patient care (**Table 1**).

#### Drug Selection

Powerful software has been developed to check whether a patient’s drug prescription conflicts with his or her insurance company’s formulary, although the benefits of this (if

**Table 1. Ten Ways Lab and Pharmacy Can Be Linked to Improve Care**

Category	Concept	Examples (Drug—Lab Pair)*	Special Role for the Computer/Linkages
Drug selection	1. Lab finding <b>contraindicates</b> drug	+ Pregnancy test—ACE inhibitor ↑SUN/Cr—metformin hydrochloride	Prevents prescription writing or dispensing
	2. Lab finding suggests <b>indication</b> for drug	↑ TSH—levothyroxine sodium ↑ Cholesterol—lipid-lowering treatment	Generates timely reminders, tracking intervention
Dosing	3. Lab finding affecting drug <b>dose</b>	↑ Creatinine—digoxin, vancomycin hydrochloride	Performs dose calculations based on age, sex, lab value, weight
	4. Drug requiring lab measure for <b>titration</b>	Warfarin sodium—PT/INR Anticonvulsants—drug levels	Statistical process control dosing adjustment charts
Monitoring	5. Abnormal lab value <b>signaling toxicity</b>	Liver enzymes—isoniazid, glitazones ↓ HCT, WBC—chloramphenicol	Triggers alert, assesses likelihood
	6. Drug warranting lab value <b>monitoring</b> for toxicity	Clozapine—WBC Amphotericin B—creatinine	Oversees scheduling of both baseline and serial monitoring tests
Lab interpretation	7. Drug <b>influencing</b> or <b>interfering</b> with lab finding	Carbamazepine—free thyroxine Quinolones—false-positive urine opiates	Warns against/interprets false-positives and false-negatives
	8. Drug <b>impacting</b> on <b>response</b> to lab finding	Insulin—↓ or ↑ glucose Penicillin—+ RPR	Resets alarm threshold for treated patients
Improvement	9. Drug toxicity/effects <b>surveillance</b>	Detects signals of previously undocumented reaction (eg, hepatotoxicity)	Data mining of lab and drug data to generate new hypotheses of drug effects
	10. Quality <b>oversight</b>	Treatment delay after abnormal results (↑ TSH, ↑ K <sup>+</sup> , + blood culture) and initiation of appropriate treatment	Monitors time interval between lab testing and prescription change, adequacy/appropriateness of lab monitoring

Abbreviations: ACE, angiotensin-converting enzyme; Cr, creatinine; HCT, hematocrit; INR, international normalized ratio; K<sup>+</sup>, potassium; lab, laboratory; PT, prothrombin time; RPR, rapid plasma reagin; SUN, serum urea nitrogen; TSH, thyrotropin; WBC, white blood cell count.

\*Plus sign indicates positive.

any) are largely financial.<sup>30,31</sup> In contrast, despite its proven clinical benefit,<sup>26</sup> few institutions have the capability of checking laboratory-based safety contraindications. For instance, a recent survey showed that no major hospital or clinic in Chicago, Ill, had mechanisms in place to automatically prevent prescribing potassium in the setting of an elevated serum potassium level, an angiotensin-converting enzyme inhibitor when a positive pregnancy test has been recorded, or metformin hydrochloride when azotemia is present (G.D.S., unpublished survey, February 2001).

On the other hand, certain clinical laboratory abnormalities represent indications for a particular drug treatment. A markedly elevated thyrotropin (TSH) level without a subsequent order for levothyroxine sodium (or a repeat test), or a repeatedly elevated glucose or hemoglobin A<sub>1c</sub> level with no hypoglycemic drug prescription, represents a laboratory abnormality mandating pharmacy actions and should generate alerts in their absence.<sup>32,33</sup>

### Dosing

A review of patients with digoxin toxicity showed that 32% had renal insufficiency, in most cases without proper dosing adjustment.<sup>34</sup> Recently, we studied medication orders for patients with decreased creatinine clearance. Among drugs that were renally excreted or nephrotoxic, 70% of orders were written for an inappropriately high dose or frequency.<sup>2</sup> Thus, despite decades of published guidelines<sup>35</sup> supplementing the explicit instructions on each drug's package label, physicians clearly need more reliable tools to ensure proper renal dosing.<sup>4</sup> It is not realistic to expect clinicians to remember the hundreds of drugs requiring altered doses as well as to think through which patients need such adjustments and to what degree. Any systematic effort to translate dosing guidelines into actual practice must automate the calculation of both creatinine clearance (which requires knowledge of patient's serum creatinine level, age, and weight) and the adjusted dos-

age. Although there is no analogous method to calculate hepatic clearance, elevated aminotransferase levels, high bilirubin level, or low albumin levels suggest that a lower dose of hepatically cleared medications is needed.<sup>36,37</sup>

In addition to initial dose selection, many drugs, such as anti-convulsants, anticoagulants, and endocrine or hormonal drugs (eg, insulin, thyroxine, erythropoietin), require ongoing titration based on measurement of serum drug levels or other clinical laboratory indicators of their biological effects. Currently, there are wide variations in testing frequency, appropriateness, and achievement of target levels.<sup>38,39</sup>

How often should such tests be done, and how should dosing be adjusted on the basis of the results? Drug-laboratory-linked computerized data facilitate graphic flow charting of laboratory results and drug dosing. Using statistical process control, a proven tool in other industries, clinicians could more scientifically respond to changes in the test results.<sup>40</sup> This method can help clinicians and even patients graph laboratory results (such as glucose or anticoagulation tests) in relation to drug dosages over time. Such charts can help determine when to modify drug dose by determining whether variation in levels is random (and drug dose should not be "tampered" with) or truly out of control (necessitating a change).<sup>41-43</sup> Using statistical process control methods, diabetic patients have been more successful at achieving target control levels than the current physician hit-and-miss approach, with one practice showing a drop in average fasting blood glucose level from 187 to 110 mg/dL (10.4 to 6.1 mmol/L) and a decrease in hemoglobin A<sub>1c</sub> concentration from 10.5% to 7.2%.<sup>44</sup>

### Monitoring

A laboratory test result could be "smarter" if it "knew" which drugs a patient was taking. For example, apparently minor liver abnormalities assume greater importance if a patient is receiving a hepatotoxic drug.<sup>37,45,46</sup> Similarly, hypokalemia

has special meaning for a patient taking digoxin.<sup>47-49</sup> Drug-laboratory interconnections need to couple information on the starting time and date of a prescription with the intelligence to interpret changes in laboratory results over time. Thus, patients' previous laboratory results become important to detect changes (not just normal or abnormal) in laboratory parameters—subtle changes that otherwise might be ignored.<sup>50</sup>

Certain drugs require baseline or scheduled laboratory monitoring. Troglitazone was removed from the US market because of infrequent (1.9/100) but potentially fatal hepatotoxicity.<sup>51</sup> The drug's manufacturer and the US Food and Drug Administration initially argued that troglitazone was safe if patients were properly monitored. However, despite a series of 4 increasingly strong warnings for liver test monitoring added to the drug's official label, a study at one academic hospital showed that less than 5% of the patients actually received the monthly testing the Food and Drug Administration warned was a precondition for safe use of the drug.<sup>7</sup> Similar failure to monitor was recently documented for statin cholesterol-lowering agents.<sup>52</sup> Considering the logistics of coordinating such drug-related laboratory monitoring, integrated computerized scheduling and tracking would appear to be a prerequisite for a safe system.<sup>53</sup>

### Laboratory Interference and Interpretation

Earlier work by Friedman et al<sup>54</sup> and Young<sup>55</sup> and more recent studies by Finnish investigators<sup>56-59</sup> (including Gronroos et al<sup>56</sup> and Forsstrom et al<sup>57</sup>) have shown the importance of the laboratory knowing which drugs the patient is taking to avoid misinterpreting results in instances where drugs interfere with laboratory measurement. One survey of specimens sent for hormone studies found that 11% were from patients currently taking one or more potentially interfering drugs, and nearly 40% of the patients tested for TSH had such conflicts.<sup>58,60</sup> This issue looms sufficiently large that the

Finnish laboratory scientists created a database cataloging their patients' drug profiles, and demonstrated improved accuracy in interpretation of their laboratory's test results.<sup>61</sup> Elsewhere, most drug-laboratory conflicts go undetected, while others are simply unknown because of scant research on in vitro laboratory interference or in vivo biologic effects.<sup>62</sup> Where conflicts have been identified, we generally lack evidence about their magnitude and clinical significance.

Even simple laboratory follow-up questions such as, "Does this glucose level of 300 mg/dL require urgent follow-up?" could be more easily answered if it was known whether the patient was taking glucose-lowering medication (ie, was a known diabetic). The response to anemia in a patient taking erythropoietin should be different from that for a falling hematocrit in a patient taking a nonsteroidal anti-inflammatory drug.<sup>63</sup> Knowing not only what drugs a patient is taking but when they were taken is important for the laboratory to interpret drug levels as well as to ensure properly timed specimen collection.<sup>39</sup>

### Learning and Improvement

Data mining with the use of powerful search algorithms and massive linked databases represents a new model for scientific research that promises to substantially improve clinical care.<sup>19,64-68</sup> Advances emerging from the Human Genome Project illustrate the enormous potential of what previously might have been considered unsystematic data collection but, when linked to phenotype data, permits discovery of new knowledge.<sup>69</sup> Similar advances in knowledge of drug effects and outcomes can result from the linking of laboratory to pharmacy. While associations between a clinical laboratory abnormality and pharmaceutical agents should be considered hypotheses for future testing, these signals can be invaluable for earlier detection of adverse drug effects.<sup>64,70</sup>

On a more mundane improvement level, laboratory-pharmacy linkages can help evaluate the timeliness of responses to abnormal laboratory results, or the adequacy or appropri-

ateness of monitoring patients taking a particular drug. This quality assurance role has been deployed to uncover inappropriate laboratory testing (orders for drug levels for patients not taking or not in a steady state for a drug, or excessively repeated levels without dose change) or to document failure to obtain recommended monitoring.<sup>71-73</sup> Mismatches in microbiology data and antibiotic prescriptions have identified patients given antibiotics to which their infections were resistant or being treated without proper cultures having been obtained.<sup>67</sup> Population diabetic outcomes can be tracked by using pharmacy records to identify diabetic patients taking hypoglycemic medications and then linking records to serial renal function.<sup>74-76</sup> Given properly linked laboratory-pharmacy databases, such questions could be evaluated for a particular drug, laboratory test, physician, or time frame (to establish historical quality trends).

## LINKING LABORATORY AND PHARMACY: CURRENT APPROACHES

### Retrospective Linkage

Retrospective electronic data have been used to perform many of the 10 functions we describe in Table 1. Even when laboratory and pharmacy data reside in separate systems and are not concurrently interfaced, these data can be retrospectively linked to better treat and protect patients.

At the simplest level, some hospitals generate reports for patients receiving prescribed drugs that require renal adjustment, then manually look up their creatinine values.<sup>77</sup> This type of drug-laboratory "bridging" function has been an invaluable contribution of clinical pharmacists, although it is labor intensive and requires "rework" that could be avoided with a prospective system. Although such reports are by definition retrospective, they have played a valuable role in identifying problem orders and improving care.<sup>78,79</sup>

A more powerful and efficient retrospective linkage involves the merging and screening of files from laboratory and pharmacy information systems. One of us (D.K.) down-

loads more than 1 million drug and laboratory records annually from the 19 Illinois state psychiatric hospitals and links them to evaluate a series of quality indicators.<sup>71</sup> "Cleaning" the data to make it usable for such screening has required extensive programming, particularly for pharmacy data. An important insight emerging from this experience is that pharmacy data files are much more complex and unstandardized than laboratory data. For example, 37 steps are required to convert the inpatient pharmacy data of the Illinois mental health pharmacy database into a standardized dosing, frequency, and duration table (laboratory data require fewer than half that number).

Outpatient pharmacy files are often less complex. Because widely available programs such as Microsoft Excel or Access can now easily import data files downloaded by information technology staff, any physician, pharmacist, or quality assurance nurse can create spreadsheets or databases that link pharmacy records with laboratory values for a given patient by means of simple sorting, filtering, and query tools. When both laboratory and pharmacy use a common patient identifying number, matching the 2 datasets is straightforward. A quality analyst can flag all records for patients meeting specified criteria and create tables that chronologically display merged laboratory and drug prescription data (**Figure**). Using this method, we uncovered more than 500 prescriptions in a single year for oral potassium supplementation (2.4% of all potassium prescriptions) written and dispensed for patients with preexisting elevated serum potassium values ( $\geq 5.3$  mEq/L).<sup>1</sup>

### Real-Time Linkage

Compared with retrospective efforts, implementation of physician order entry systems and electronic integration of laboratory and pharmacy data that allow real-time decision support can have even greater benefits in each of our 10 conceptual realms.<sup>80</sup>

When a laboratory test affects a drug dose, displaying key laboratory information at the time a drug

is ordered or when a pharmacist enters the order into the computer (eg, showing last phenytoin level when phenytoin is ordered) can help clinicians make better decisions.<sup>81</sup> The computer can calculate an appropriate dose based on the patient's renal function, age, sex, and weight. One study evaluating the impact of renally adjusted dosing in hospitalized patients found that such decision support improved dosing appropriateness from 54% before the intervention to 67% afterward.<sup>2</sup>

Titration of medications with the results of laboratory testing is one of the domains in which computerized decision support has been found to be particularly helpful.<sup>82</sup> For example, interactive computerized assistance with warfarin dosing has been shown to improve the proportion of time a patient spends within the therapeutic range.<sup>83</sup> In addition, for many medications for which drug level monitoring can be performed, these results can be used to make suggestions about when another level should be checked. Decision support can reduce the number of redundant levels by estimating the appropriate monitoring interval.<sup>38,84,85</sup> In one study, more than 80% of antiepileptic drug levels were found to be inappropriate, and many would have been avoided if real-time warnings had been presented at the time the test was being ordered.<sup>39,81</sup>

When laboratory tests signal drug toxicity, studies have shown that the computerized alerts can be used to limit the extent of an adverse drug event and enhance the timeliness of interventions to minimize its harm.<sup>86,87</sup> As the computer detects a critical laboratory result for a patient receiving a particular drug, warnings are generated for a pharmacist to intervene or, more powerfully, such results are being communicated immediately to providers electronically by means of tools such as 2-way pagers.<sup>88</sup>

Computerized decision support has also been shown to increase the likelihood that appropriate monitoring will occur. Overhage and coworkers' study<sup>89</sup> of "corollary orders"—situations in which one order implies another—demonstrated that decision support dramatically in-

NAME	UNITNO	DATE	RESULT	GENERIC_NM	QUANTITY
JONES, BILL	122441	03/11/95	6.0		
JONES, BILL	122441	03/20/95		POTASSIUM CHLORIDE	60
SMITH, MARY	125565	05/16/95	5.3		
SMITH, MARY	125565	05/16/95		POTASSIUM CHLORIDE	30
SMITH, MARY	125565	11/19/95	7.0		
STOKES, WILL	137995	01/03/95		POTASSIUM CHLORIDE	30
STOKES, WILL	137995	01/03/95	5.3		
CULLEN, CORA	148341	03/30/95	5.3		
CULLEN, CORA	148341	04/01/95		POTASSIUM CHLORIDE	14
CULLEN, CORA	148341	04/12/95		POTASSIUM CHLORIDE	60
CULLEN, CORA	148341	06/14/95		POTASSIUM CHLORIDE	30
PABST, POLLY	155103	01/11/95	5.3		
PABST, POLLY	155103	04/12/95		POTASSIUM CHLORIDE	240
KENNEDY, JOE	156828	02/22/95	5.6		
KENNEDY, JOE	156828	03/06/95		POTASSIUM CHLORIDE	240
KENNEDY, JOE	156828	04/05/95	4.9		
KENNEDY, JOE	156828	05/09/95	6.6		
KENNEDY, JOE	156828	05/10/95		POTASSIUM CHLORIDE	20
KENNEDY, JOE	156828	05/23/95	5.2		
KENNEDY, JOE	156828	05/24/95		POTASSIUM CHLORIDE	30

Examples of actual errors disclosed when pharmacy records and laboratory data were merged and then sorted by patient and date. For example, the first record/row is from the laboratory computer, and the second is from the pharmacy database (patient names and clinic numbers changed).

creases the likelihood that recommended laboratory monitoring orders were written. Compliance rates of indicated monitoring (baseline and follow-up platelet count and activated partial thromboplastin time) for patients receiving heparin increased from 40.2% (control subjects) to 77.4% in patients whose physicians were presented with reminders coupled with streamlined ordering screens for laboratory tests linked to drug orders.<sup>89</sup>

Decision support can be critical when a laboratory test contraindicates a certain medication. When a patient is pregnant, angiotensin-converting enzyme inhibitors are contraindicated. However, most systems do not capture a positive pregnancy test, especially if performed by the patient at home. Such information would also need to be enhanced with simple rules (eg, pregnancy does not last longer than 10 months; after a delivery a woman is no longer pregnant) to keep it dynamically updated.

Some situations are more complex to handle electronically because they are asynchronous.<sup>90</sup> For example, while a high TSH level often indicates that an action should be taken (eg, adding or increasing the dose of levothyroxine), it often registers after (rather than during)

an outpatient encounter. Implementation of one inpatient ordering system linking medications and laboratory resulted in a 38% decrease in the median time interval to act on critical laboratory results.<sup>91</sup>

Finally, combined elements of retrospective and real-time decision support have proved useful for providing quality oversight and improvement. Several studies have demonstrated that drug-laboratory combinations are one of the best tools for identifying adverse drug events, in both the inpatient and outpatient settings.<sup>92-95</sup> Relying to a large extent on laboratory signals suggesting an adverse event, Classen et al<sup>92</sup> demonstrated an 800% increase in the number of adverse drug events identified compared with the standard approach (spontaneous reporting). Because such an approach to screening for adverse drug events is so much more efficient (more problems detected with less effort), it has made continuous monitoring, previously unsustainable, possible.<sup>93</sup>

Development of systems that ensure appropriate follow-up of a specific abnormality or laboratory-pharmacy signal is critical for achieving error-free tracking and accountability. Many studies demonstrate that abnormal results often do not receive timely or appropriate follow-up.<sup>3,91,96</sup> Linked systems facili-

**Table 2. Labeled Laboratory-Pharmacy Interactions\***

Laboratory Result	Top 40 Drugs		New Drugs (n = 37)	
	Total Warnings	No. of Drugs With Warning	Total Warnings	No. of Drugs With Warning
Contraindication for drug	11	9	20	14
Indication for drug	7	7	3	3
Dose adjustment	40	31	28	23
Indicating toxicity	169	39	161	32
Baseline monitoring	16	11	12	8
Follow-up monitoring	20	11	16	10
Interfered with by drug	5	3	2	2
<b>Total</b>	<b>268</b>	<b>40</b>	<b>242</b>	<b>37</b>

\*As listed in the 2000 *Physicians' Desk Reference*.<sup>97</sup> Official Food and Drug Administration labeling for oral dosage medications was evaluated. Top 40 drugs were based on 2000 IMS data. New drugs were based on new molecular entities newly approved by the Food and Drug Administration and marketed in 1999 and 2000.

tate both review by an individual provider and systemwide quality oversight by enabling organized systems for intervention when clinicians fail to follow up.

#### WHAT TO LINK: NEED FOR STANDARDS AND RESEARCH

The current evidence base is thin regarding which tests to link and at what thresholds. While many of the examples we discuss appear to be reasonable starting places, our taxonomy is merely an entry point for future research.

One information source for prescribers to consider is the official Food and Drug Administration drug labeling—warnings to which, in theory, they are legally obliged to pay heed. These “labeled” instructions appear on the prescriber package inserts and are reprinted in the *Physicians' Desk Reference*.<sup>97</sup> In **Table 2** we summarize laboratory-pharmacy interactions listed in the *Physicians' Desk Reference* for the most commonly prescribed, and the recently approved, oral medications. There are more than 500 laboratory-pharmacy interactions—an average of 6.6 per drug. These interactions, with their associated requirements and warnings, are so numerous that it is unlikely that any unaided physician could remember and manually track all of them simultaneously for all the drugs prescribed for his or her patients.

However, linked alerts will not be effective if users are overloaded

with a “blizzard” of poorly validated warnings. This point has been illustrated by pharmacists' experience of being deluged with a large number of computerized warnings of drug-drug interactions, many of which are not evidence-based or consistent among different commercial software products.<sup>98</sup> As a result, important warnings are overlooked, and pharmacists inactivate many of the alerts.<sup>99,100</sup> Indiscriminantly adding hundreds of drug-laboratory interactions could further lead pharmacists and physicians to ignore or inactivate many of the warnings. A research agenda is very much needed to help sort out the usefulness of various tests, thresholds, and actions.<sup>101</sup>

#### FUTURE CHALLENGES

Paraphrasing Donabedian's triad,<sup>102</sup> (1) setting up the electronic infrastructure, (2) creating standardized laboratory-pharmacy linkage processes and clinical rules, and (3) demonstrating the benefit of such linkages on patient outcomes all pose major challenges.

Progress in real-time ordering and feedback has been inhibited by the cost of implementing full-scale linked information systems. Many physicians have been reluctant to invest in the additional dollars and have further concerns about perceived added time burdens. Even where computerized ordering is in place, building and maintaining the knowledge base is challenging, especially as increasingly complex decision sup-

port is attempted. A recent survey of institutions that have installed commercial systems with order entry found that less than 10% were using “intelligent” rules that linked information from different systems such as laboratory and pharmacy.<sup>103</sup>

A major problem has been that, lacking standardized and tested drug-laboratory interaction rules, each institution finds itself reinventing the wheel. Although vendors advertise packages of ready-to-use rules, none of these (either individual rules or rule sets) has been subjected to formal testing or peer review. The effort associated with maintenance must be underscored, especially given the large numbers of medications being introduced each year. Thus, a public compendium of evidence-based rules would be extremely valuable.

In the future, pharmacogenomics, laboratory's newest emerging domain, will add a further level of challenge and complexity.<sup>104</sup> Evidence suggests, for example, that certain genotypes, such as allelic variants of cytochrome P450, can substantially alter patients' response to warfarin or the likelihood of having a hypersensitivity reaction to phenytoin. This pushes the boundaries of laboratory-pharmacy interactions, potentially redefining as “preventable errors” more and more reactions currently deemed to be “idiosyncratic,” as well as moving us toward patient-specific targeting of drug actions.<sup>105,106</sup>

#### CONCLUSIONS

While much has been written about “managed care,” effectively managing clinical care for both inpatients and outpatients demands better integration of clinical laboratory and pharmacy data. The evidence that existing data are not being optimally used is substantial, and accessible solutions exist today that can significantly improve care. While more advanced technologies in the future hold great promise, given the demonstrated and potential benefits for the laboratory, pharmacy, clinician, and patient, the case for immediate efforts to link laboratory and pharmacy information is compelling.

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