

# Electronic Medical Record Prompts for Lab Orders in Patients Initiating Statins

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## Keywords

Computerized medical records, ambulatory care facilities, clinical laboratory techniques, statins, HMG-COA

## Summary

**Background:** The Institute of Medicine (IOM) reports that at least a fourth of all medication related injuries are preventable. Therefore, the IOM recommends healthcare organizations and providers implement electronic prescribing and clinical decision support systems in practices to aid in medication error prevention.

**Objective:** To assess the impact of noninvasive-intrusive prompts from an electronic medical record on recommended baseline and follow up laboratory monitoring, CK and liver transaminase levels (AST and ALT), in patients initiated on statin therapy.

**Methods:** Hybrid noninvasive-intrusive prompts for laboratory monitoring specific for statin initiation were implemented in the electronic medical record system in a community based, university affiliated family medicine residency program. A retrospective chart review was conducted to compare and assess laboratory monitoring in patients initiated on statin therapy from two specific time periods: a six month period prior to initiation of the prompts and a six month period after initiation of the prompts.

**Results:** One hundred seventy three patients met inclusion criteria. There were no significant differences in assessment of baseline liver transaminases and CK levels from the initial study period to the follow up study period. There were significant differences in follow up liver transaminase levels (18% vs 33%,  $p = 0.035$ ) and CK levels (none vs 7%,  $p = 0.03$ ) from the initial study period to the activated prompt interval.

**Conclusion:** A hybrid noninvasive-intrusive specific prompts for laboratory monitoring triggered by statin initiation within an electronic medical record improved follow up lab assessments for liver transaminases and CK but did not improve baseline assessments of CK or liver transaminases.

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## Appl Clin Inf 2011; 1: 104–115

doi: 10.4338/ACI-2010-07-RA-0044

received: July 26, 2010

accepted: February 10, 2011

published: March 16, 2011

**Citation:** Carroll DG, Alexander C, Radford EA, Leeper J, Carroll DN. Electronic medical record prompts for lab orders in patients initiating statins. *Appl Clin Inf* 2011; 2: 104–115

<http://dx.doi.org/10.4338/ACI-2010-07-RA-0044>

## Background

The Institute of Medicine (IOM) published a report in 2006 which cited that at least a fourth of all medication related injuries are preventable [1]. Electronic prescribing and clinical decision support systems are cited by the IOM as two of the most efficacious medication prevention error strategies in hospitals [1]. Due to this, the IOM recommends healthcare organizations and providers implement electronic prescribing and clinical decision support systems in practices to aid in medication error prevention. While most of the efficacy data on medication error prevention strategies are in hospitals [1, 2], it is critical healthcare providers address and assess medication error prevention strategies in ambulatory care settings to determine if these same strategies utilized in hospitals are effective in reducing medication errors in this setting.

A subset of medication errors occur when a prescriber fails to monitor laboratory values as recommended at baseline and/or at appropriate intervals with continuation of a medication. Failure to have this critical information in the presence of significant elevations in laboratory values could result in prescribers initiating or continuing medications inappropriately. It is estimated that laboratory monitoring recommendations associated with medications are not followed in 27-91% of patients based on the published literature [3-11].

The 3-hydroxy-3-methylglutaryl coenzyme A (HMG CoA) reductase inhibitors (statins) are a class of medications that have the potential to be inappropriately initiated and/or continued without checking for elevated baseline laboratory values or elevated follow up laboratory values. While statins have proven to be relatively safe drugs for treatment of hyperlipidemia as well as for prevention of major coronary events (defined as nonfatal myocardial infarction, coronary revascularization, coronary heart disease associated deaths, fatal and nonfatal stroke and transient ischemic attacks), several adverse effects associated with statin therapy require specific monitoring and follow-up [12, 13]. Myopathies (0.08%) and increased liver transaminase levels (0.5-2.0%) have been associated with statin therapy [13, 14]. The Adult Treatment Panel III (ATP III) recommends obtaining a baseline creatine kinase (CK) level prior to statin initiation, and a follow-up level if the patient experiences pain, myalgia, or weakness [12]. Increases in liver transaminase levels are associated with injury or damage to the liver. Liver transaminase levels include alanine aminotransferase (ALT) and aspartate aminotransferase (AST). ATP III recommends obtaining liver transaminase levels prior to initiation of treatment with all statins, 12 weeks after initiation of treatment, then annually thereafter [12].

Electronic prescribing and clinical decision support and prompting could assist in increasing laboratory monitoring [15-18]. However, the published data is conflicting. A few studies demonstrated no improvement especially with noninvasive prompts [19, 20].

Intrusive prompts within electronic medical record systems require a specific action (eg. canceling the alert message, changing the order, or giving a reason to continue as is) by the user before any other work can be completed. Noninvasive prompts do not require action by the user before work can be completed. Intrusive prompts have the potential to be very disruptive to work flow and can be very frustrating for the user if not clinically relevant [21-23]. This could result in users ignoring prompts if they are continuous and not clinically relevant. Noninvasive prompts are less likely to interrupt work flow, but also have the potential to be ignored by the user since no action is required. There are some electronic medical records and systems that have a hybrid mix of noninvasive-intrusive systems (an eg, MedInformatix, Inc [24]).

## Objective

We wanted to assess if a noninvasive-intrusive hybrid prompt system could assist prescribers with laboratory monitoring associated with medication use. The objective of this study to assess the impact of prompts from an electronic medical record (EMR) on recommended baseline and follow up laboratory monitoring, CK and liver transaminase levels (AST and ALT), in patients initiated on statin therapy.

## Methods

The study used an intervention design, retrospective chart review to determine the effect of prompts in the ordering module of the EMR for increasing the frequency of baseline and follow up laboratory assessments in patients initiated on statins.

## Setting and Subjects

The study took place in a community based, university affiliated family medicine residency program located in a small urban area in west Alabama. There are 8 full time faculty and 2 part time faculty within the family medicine department and there are a total of 36 residents in the program each year (12/12/12 residency program). The patients in the clinic primarily live in seven surrounding counties, population 334,131. A large, state university is located in the same county as the residency program. The surrounding counties however, are some of the poorest in the state. The active patient base in the clinic is approximately 5,700.

All of the family physicians (faculty and residents) are required to utilize the clinic's EMR for every patient encounter. The family medicine clinic averages approximately 25,000 patient encounters annually. Each patient's EMR chart contains the following information: patient care notes from each family medicine physician clinic encounter, laboratory values (in house as well as those scanned from outside providers), scanned consult notes from outside providers, and prescriptions. In addition, all orders (laboratory, prescriptions, referrals, etc) are generated and retained within the chart for each patient in the EMR.

Patients were included in the study if they were seen in the outpatient family medicine clinic, were greater than 18 years of age and were initiated on any of the following statin medications during either data collection period (Oct 1, 2006 - March 30, 2007 or May 1, 2008 - Nov 1, 2008): atorvastatin, fluvastatin, lovastatin, pravastatin, rosuvastatin, simvastatin, amlodipine/atorvastatin or ezetimibe/simvastatin. Patients were excluded if they were being treated with any statin (previously listed) within 30 days of the new statin initiation or were pregnant.

## Intervention/Laboratory prompt description

In April 2008, a series of prompts were implemented in our electronic medical record system for all new statin prescriptions entered. When any physician entered a new prescription for a statin medication (see previous list above), the electronic medical record automatically generated a prompt in the ordering section of the chart (► Fig. 1). This was nonintrusive to the physician at the time the prescription was generated. The physician did not see the prompt to order a baseline CK or liver transaminase levels as he or she was entering the new prescription into the electronic medical record. However, if and when the physician opened the ordering section of the chart, the prompt was presented recommending the provider order a baseline CK and baseline complete metabolic panel, which included liver transaminase levels. These prompts required action by the provider to either accept the recommendation and order the labs recommended or delete the recommendation. These prompts are considered intrusive since they required action by the provider at the time they presented. Any time seven weeks after the statin was initiated, the electronic medical record generated another prompt recommending the provider order follow up liver transaminase levels. Again, this prompt was only viewed by the provider if and when the ordering section of the chart was opened. As before, it required the provider to either accept the recommendation and place the order for the lab or delete the recommendation.

## Data collection

All data were collected retrospectively by chart review. The data collection period for each patient meeting inclusion/exclusion criteria was six months total, beginning from the day the statin therapy was initiated. Patients were identified through a query of the electronic medical record for statin initiation (see previous list above) during each of the data collection periods. A standardized data collection form was developed and used to collect patient information. Four trained research asso-

ciates collected the data from the electronic medical record. Inter-rater reliability checks were performed by the lead investigator periodically throughout the data collection process.

## Data analysis

The objective of this study to assess the impact of prompts from an electronic medical record on recommended baseline and follow up laboratory monitoring in patients initiated on statin therapy. We assessed whether or not baseline CK and liver transaminase levels were obtained. CK and liver transaminases obtained within 48 hours of initiation were considered baseline. We also assessed whether follow up liver enzyme levels or CK levels were obtained. Liver transaminase levels obtained seven to 24 weeks after statin therapy was initiated were considered follow up and CK levels reassessed anytime 48 hours after statin initiation were considered follow up.

There were two unique data collection periods which were analyzed for comparison. One period after statin therapies were initiated, the initial period, was prior to prompts being implemented in the electronic medical record (baseline: Oct 1, 2006 - March 30, 2007). The other period after statin therapies were initiated, the activated prompt interval, was after the prompts were implemented (April 1, 2008) in the electronic medical record (follow up: May 1, 2008 - Nov 30, 2008).

The study outcomes were analyzed according to the intention to treat principle. A chi squared test was utilized to assess categorical variables. A student's t test was utilized to assess continuous variables. Statistical significance was set a priori at  $<0.05$  (all p values are two sided).

## Results

One hundred seventy three patients met inclusion criteria for the study. There were 61 patients in the period prior to implementation of prompts in the electronic medical record and 112 in the period after implementation of prompts in the electronic medical record. The groups were well balanced in the both study periods with the exception of specialists were writing statin prescriptions more in the initial study period than the activated prompt interval (▶ Table 1).

Statin prescribing was also analyzed. Groups were well balanced in regards to the statin prescribed in both study periods (▶ Table I). However, simvastatin was prescribed more than any other statin by providers in both study periods and significantly more in the activated prompt interval ( $p = 0.047$ ). Simvastatin was likely prescribed more frequently than the other statins for several reasons: available generically, the statin of choice on the state Medicaid plan and has outcomes data for cardiovascular prevention.

For the initial study period (prior to implementation of lab prompts), 3% ( $n = 2$ ) of charts reviewed received monitoring of baseline CK compared to 12% ( $n = 13$ ) in the activated prompt interval (after implementation of lab prompts),  $p = 0.06$  (▶ Table 2 for results). Baseline liver transaminase levels were assessed in the initial study period in 41% ( $n = 25$ ) of patients compared to 46% ( $n = 52$ ) in the activated prompt interval,  $p = 0.49$ . No AST or ALT measurements were greater than two times the upper limit of normal at baseline throughout the study. In addition, there were no elevated CK levels at baseline in any patients.

CK was assessed as follow up in 7% ( $n = 8$ ) of patients in the activated prompt interval compared to none in the initial study period,  $p = 0.03$  (▶ Table 2 for results). Four of those patients had slightly elevated CK above upper limits of normal for our laboratory ranges. 18% ( $n = 11$ ) of patients were monitored with follow-up liver transaminase levels in the initial study period compared to 33% ( $n = 37$ ) in the activated prompt interval,  $p = 0.035$ . There were no AST or ALT measurements greater than three times the upper limit of normal in follow up assessments. Of those patients with follow-up liver transaminase monitoring, the mean number of weeks between statin initiation and follow up assessment was 15.33 ( $\pm 7.4$ ) weeks in the initial study period and 16.65 ( $\pm 5.45$ ) in the activated prompt interval.

## Discussion

This study is unique in that it assessed use of a hybrid nonintrusive-intrusive specific prompts for laboratory monitoring triggered by specific drug class (statin) initiation with in an electronic medical record. The current literature [2, 15-18] supports use of intrusive prompts as those can significantly improve laboratory monitoring of prescribed medications. A Cochrane review assessed 28 trials regarding point of care computer reminders and their impact on processes and outcomes of care. 13 of the 28 assessed test ordering. The absolute median improvement in test ordering from these trials was 3.8% (interquartile range of 0.4 to 16.3%) and the absolute best improvement based on the data from these trials was 9.6% (interquartile range 0.6% to 24%) [2]. While intrusive prompts have benefit, the literature [19, 20] reports an insignificant impact from use of nonintrusive prompts in improving laboratory monitoring with prescribed medications. The hybrid nonintrusive-intrusive prompt system utilized for this study had diverse results.

The laboratory prompts generated in the electronic medical record by a new statin prescription did significantly improve follow up monitoring of liver transaminase levels (▶ Table 2). These results (15% improvement) are similar to or slightly higher (0.4 to 24% improvement) than what has been previously reported in the literature for intrusive prompts [2, 15-18]. However, the prompts did not significantly improve baseline assessments of CK levels or liver transaminase levels (▶ Table 2). These results are similar to results from nonintrusive prompt trials [19, 20]. One reason the prompts for baseline labs may not have significantly impacted physician ordering could be the prompts in our system were both nonintrusive and intrusive. If the physician failed to go to the ordering module in the chart on the day the statin was initiated, he or she would not have had the opportunity to be prompted to order the baseline CK or liver transaminases based on the prompt system in our EMR.

One should also consider the impact and unintended consequences that computerized order entry (COE) and prompts have on health care providers. Ash and colleagues have published two trials that explore these issues within hospital systems, but there currently is no data assessing these issues in an outpatient clinic setting [21, 22]. Based on their research, there have been two domains in which these unintended consequences fall: content and presentation [22]. Ash and colleagues report that issues related to content typically fall into one of the following three categories: elimination or shifting of human roles, currency (up to date) of the system, wrong or misleading content in the system. In addition, presentation issues typically fall into one of the following areas: rigidity of the system (to easily collect/track data), alert fatigue and sources of potential errors due to system functionality/set up. While these issues have only been assessed in hospital systems with COE, most of the issues should also apply to an outpatient setting. That said, there could be unique issues and consequences outpatient providers may experience with COE or issues/consequences that have a greater impact in an outpatient setting that need to be identified and further assessed. Based on our experiences, we believe we had greater issues with presentation, namely alert fatigue and potential errors due to system functionality/set up, rather than content.

There are multiple limitations to this study. If the statin was initiated by physician outside of the practice, we were unable to identify whether or not the patient was being monitored by the prescribing physician. This is an everyday challenge many family physicians consistently deal with in their practices. Until there is an easier way to share information (like laboratory data, test results, consult notes, etc) between EMR systems or providers in “real time”, this will continue to be problematic. In this study, 45% of statins were initiated by a physician outside of the practice in the initial study period compared to 24% in the activated prompt interval,  $p = 0.006$ . This significant decrease in outside physician providers initiating statins in our patients in the follow up period could be a potential confounder in this study.

Another limitation of this study was that 42% of patients did not follow up at all after statin initiation in the initial study period compared to 30% in the activated prompt interval period ( $p = 0.10$ ) giving the physician no opportunity to draw follow-up labs. Our analysis was conducted per ITT, therefore, we assumed if the patient did not follow up in our clinic no laboratory monitoring was conducted regarding the statin therapy. This type of analysis could have impacted our results (conservative estimation) yet is realistic to what many healthcare providers deal with on a daily

basis in their practices. In each study period, all patients had at least one visit to their primary care physician. The average number of visits to their family physician in the 6 months following statin initiation was 1.7 in the initial study period and 1.7 in the activated prompt interval period,  $p = 0.86$ . However, when patients who failed to come back in for follow up were excluded, the average number of visits to their family physician in the 6 months following statin initiation increased to 2.9 in the initial study period and to 2.5 in the follow up study period,  $p = 0.30$ . The more frequent patient follow up occurred, the more opportunities the physician had go into the ordering section of the chart to see the prompts for lab monitoring.

In addition, we were not able to assess if the lab tests were ordered yet patients failed to follow through with actually going to the laboratory to have a sample drawn in order for the test to be conducted. We believe these numbers would be small though since our laboratory is located in house and convenient for our patients to access immediately prior to or following a physician visit. In addition, all orders for laboratory monitoring are generated and transmitted electronically within the EMR. Based on this, we do not believe this data would have significantly altered our results but should be considered in future trials.

Finally, there were more patients enrolled meeting inclusion criteria in the activated prompt interval ( $n = 112$ ) compared to the initial study period ( $n = 61$ ). This could be a potential confounder. The reason for this difference in new prescriptions for statins initiated is not clear.

One way to help ensure follow-up labs are being monitored in patients who had statin therapy initiated by physicians outside of the practice, which is common in family medicine practices today, is to have patients sign releases for medical information to be exchanged between specific providers and then request the labs from the prescribing physician. Exchange of information in “real time” regarding patient data (test results, laboratory values, notes, etc) from another provider at the time a physician is with a patient in a visit, could significantly improve care since the physician would have more complete information available to make decisions in a timely manner. If there are no follow-up labs available, the family physician could order the appropriate tests needed. In addition, there are several other prompts that appear in the ordering module for other disease states and wellness/prevention measures. An average of 8 prompts appears per patient encounter in the ordering system based on the current EMR set up. The lab tests could have been “ignored” or “deleted” with the other prompts in the system that day due to time constraints. As previously stated, this is a known unintended consequence identified in the literature that we believe could have impacted our providers and thus our results [2, 21-23].

The issue of patient follow-up could be addressed by calling patients as their follow-up date approaches to remind them to come to clinic [25-27]. Another idea would be to issue appointment cards to the patients that they could take with them when they leave clinic, or that could be mailed to them to remind them to come in for follow-up laboratory tests and appointment [27, 28]. In addition, the family physician could encourage patient follow-up by only writing prescriptions for a 3 month supply, requiring the patient to follow up in clinic to get a new prescription.

Finally, based on our experiences, there are several things on our “wish list” to improve functionality of our EMR as well as exchange of information between providers. First, immediate interface with our prescription and ordering sections to current and past laboratory data in our EMR database that is clinically relevant and which is automatically displayed at time of generation of the order (prescription, test, lab, etc). This immediate access to clinically relevant information with minimal “work” to navigate to that data by the provider would improve work flow and could provide clinically meaningful data to guide decisions. Second, lack of prompt generation if data is currently in the EMR and the standard, as established by the providers, has been met (eg, baseline labs are already in the system and/or are within normal limits at baseline and/or follow up) to minimize alert fatigue. This is not only for lab data but other prompts that are generated for health maintenance in our system (tests, vaccinations, etc). Finally, real time interface to access health records/data with other providers not in our EMR system so that tests are not duplicated and information (test results, notes, etc) is shared in a timely and relevant manner related to provision of actual patient care in the office.

## Conclusion

This study demonstrated that hybrid noninvasive-intrusive specific prompts for laboratory monitoring triggered by statin initiation with in an electronic medical record improved follow up lab assessments for liver transaminases and CK but did not improve baseline assessments of CK or liver transaminases. Further assessment of prompts, both intrusive and nonintrusive, in electronic medical records in outpatient settings is needed to determine how effective they would be to help prevent potential medication errors.

## Implications of the results

Previously in our residency program, intrusive prompts were used to remind physicians of multiple preventive care measures and evidence-based interventions. Unfortunately, there were so many intrusive prompts, that the physicians ignored the prompts altogether (unpublished data). Fortunately, in this study hybrid non-intrusive intrusive prompts were shown to be effective in modifying physician behavior. Specifically, the prompts were effective in improving monitoring of lab values on patients placed on a high risk drug.

Using electronic prompts to improve care will become increasingly more important as the number of evidence-based interventions for chronic disease increases exponentially. As the IOM report said in 2001, there is simply more information available than physicians can retain and act meaningfully on [29]. Electronic support for evidence based medicine will be critical moving forward. As physicians struggle to use EMRs effectively, and meaningfully, these results are promising in providing decision support for physicians.

### Conflicts of interest

None of the authors have any conflicts of interest – financial or personal relationships – that could influence or bias the objectivity of this study and content within this manuscript. We received no funding to conduct this study or to submit this manuscript.

### Protection of human subjects

The study was approved by the university Institutional Review Board and is in compliance with the Declaration of Helsinki.

Order	Dx	ICD9	Status	Last Done	Note
<input type="checkbox"/> Womens Health					Womens Health
<input checked="" type="checkbox"/> Pap,Liquid w HPV Reflex[88142]	Well Pt	V76.2	New	Never	Well Pt 3 yr Pap Smear
<input checked="" type="checkbox"/> Vaccines					Vaccines
<input checked="" type="checkbox"/> Diabetes					Diabetes
<input checked="" type="checkbox"/> COPD					COPD
<input checked="" type="checkbox"/> Statin Patient					Statin Patient
<input checked="" type="checkbox"/> Comprehensive Metabolic[80053]	Statin Pt.	V58.69	New	Never	Initial/Chgd statin For: initial test: CMP (or BUN)
<input checked="" type="checkbox"/> CK-Total[82550]	Statin Pt.	V58.69	New	Never	Initial/Chgd statin For: initial test: CK-Total

Fig. 1. Prompt Within the Electronic Medical Record

**Table 1** Patient Demographics

	<b>Prior to Prompt Implementation N = 61 (n/%)</b>	<b>After Prompt Implementation N = 112 (n/%)</b>	<b>P value</b>
<b>Gender n/%</b>	26/43% Male	49/44% Male	0.89
<b>Average Age (± SD)</b>	56.4 (± 16.5)	54.7 (± 13.3)	0.47
<b>Insurance/Payor Status</b>			
<b>Private insurance</b>	34/56%	50/45%	0.30
<b>Medicaid</b>	5/8%	15/13%	
<b>Medicare</b>	16/26%	36/32%	
<b>Medicaid and Medicare</b>	2/3%	8/7%	
<b>Self Pay</b>	4/7%	3/3%	
<b>Primary Care Provider</b>			
<b>Family Medicine Intern</b>	8/13%	18/16%	0.91
<b>Family Medicine Postgraduate year 2</b>	18/29.5%	30/27%	
<b>Family Medicine Postgraduate year 3</b>	18/29.5%	36/32%	
<b>Family Medicine Attending</b>	17/28%	28/25%	
<b>Specialist physician written prescription for statin</b>	28/45%	27/24%	0.003
<b>Statin Prescribed</b>			
<b>Simvastatin</b>	28/46%	69/62%	0.047
<b>Atorvastatin</b>	14/23%	24/21%	0.14
<b>Fluvastatin</b>	1/1%	None	
<b>Lovastatin</b>	3/5%	2/2%	
<b>Pravastatin</b>	3/5%	1/1%	
<b>Rosuvastatin</b>	6/10%	11/10%	
<b>Atorvastatin and amlodipine</b>	None	1/1%	
<b>Simvastatin and ezetimibe</b>	6/10%	4/3%	

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**Table 2** Results

Outcome	Prior to Prompt Implementation (Initial Study Period) N = 61 (n/%)	After Prompt Implementation (Activated Prompt Interval) N = 112 (n/%)	P value
<b>Baseline</b>			
CK assessed	2/3%	13/12%	0.06
Liver transaminase levels assessed	25/41%	52/46%	0.49
<b>Follow up</b>			
CK assessed	None	8/7%	0.03
Liver transaminase levels assessed	11/18%	37/33%	0.035

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## References

1. Preventing medication errors: quality chasm series. Aspden P, Wolcott J, Bootman JL, Croenewett LR, editors. [http://books.nap.edu/openbook.php?record\\_id=11623](http://books.nap.edu/openbook.php?record_id=11623). Accessed: November 29, 2010.
2. Shojania KG, Jennings A, Mayhew A, Ramsey CR, Eccles MP, Grimshaw J. The effects of onscreen, point of care computer reminders on processes and outcomes of care. *Cochrane Database Systematic Reviews* 2009; 3: CD001096.
3. Schoenenberger RA, Tanasijevic MJ, Jha A, Bates DW. Appropriateness of antiepileptic drug monitoring. *JAMA* 1995; 274: 1622-1626.
4. Roblin DW, Nielsen DM. Assessment of quality in adult primary care: developing process measures from administrative data. *Clin Perform Qual Health Care* 1994; 2: 200-208.
5. Graham DJ, Drinkard DR, Shatin D. Study of liver enzyme monitoring in patients receiving troglitazone. *Pharmacoepidemiol Drug Saf* 2000; suppl 1: S131.
6. Emalie-Smith AM, Boyle DI, Evans JM, Sullivan F, Morris AD. Contraindications to metformin therapy in patients with type 2 diabetes: a population based study of adherence to prescribing guidelines. *Diabet Med* 2001; 18: 483-488.
7. Abookire SA, HArson AS, Fiskio J, Bates DW. Use and monitoring of "statin" lipid lowering drugs compared with guidelines. *Arch Intern Med* 2001; 161: 53-58.
8. Tegeder I, Levy M, Muth-Selbach U, Oelkers R, Neumann F, Dormann H. Retrospective analysis of the frequency and recognition of adverse drug reactions by means of automatically recorded laboratory signals. *B J Clin Pharmacol* 1999; 47: 557-564.
9. Selby JV, Ettinger B, Swain BE. First 20 months experience with the use of metformin for type 2 diabetes in a large HMO. *Diabetes Care* 1999; 22: 38-44.
10. Calabrese AT, Coley KC, DaPos SV, Swanson D, Rao RH. Risk of lactic acidosis with metformin therapy. *Arch Intern Med* 2002; 162: 434-437.
11. Graham DJ, Drinkard DR, Shatin D, Tsong Y, Burgess MJ. Liver enzyme monitoring in patients receiving troglitazone. *JAMA* 2001; 286: 831-833.
12. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Third report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation and treatment of high blood cholesterol in adults (Adult Treatment Panel III), Final Report. Accessed at [http://www.nhlbi.nih.gov/guidelines/cholesterol/atp3\\_rpt.htm](http://www.nhlbi.nih.gov/guidelines/cholesterol/atp3_rpt.htm) on September 4, 2007.
13. Grundy SM, Cleeman JI, Merz NB, Brewer HB, Clark LT, Hunninghake DB, et al. Implications of recent clinical trials for the National Cholesterol Education Program Adult Treatment Panel III guidelines. *Circulation* 2004; 110: 227-239.
14. Pasternak RC, Smith SC, Bairey-Merz CN, Grundy SM, Cleeman JI, Lenfant C; ACC/AHA/NHLBI clinical advisory on the use and safety of statins. *Journal of the American College of Cardiology* 2002; 40(3): 567-572.
15. Balas E, Weingarten S, Garb CT, Blumenthal D, Boren SA, Brown GD. Improving preventive care by prompting physicians. *Arch Intern Med* 2000; 160: 301-308.
16. Raebel MA, Lyons EE, Andrade SE, Chan KA, Chester EA, Davis RI, et al. Laboratory monitoring of drugs at initiation of therapy in ambulatory care. *J Gen Intern Med* 2005; 20: 1120-1126.
17. Feldstein AC, Smith DH, Perrin N, Yang X, Rix M, Raebel MA, et al. Improved therapeutic monitoring with several interventions. *Arch Intern Med* 2006; 166: 1848-1854.
18. Steele AW, Eisert S, Witter J, Lyons P, Jones MA, Gabow P, et al. The effect of automated alerts on provider ordering behavior in an outpatient setting. *PLoS Med* 2005; 2(9): e255.
19. Lo HG, Matheny ME, Seger DL, Bates DW, Gandhi TK. Impact of non-interruptive medication laboratory monitoring alters in ambulatory care. *J Am Med Inform Assoc* 2009; 16: 66-71.
20. Palen TE, Raebel M, Lyons E, Magid DM. Evaluation of laboratory monitoring alerts within a computerized physician order entry system for medication orders. *Am J Manag Care* 2006; 12: 389-395.
21. Ash JS, Sittig DF, Campbell EM, Guappone KP, Dykstra RH. Some unintended consequences of clinical decision support systems. *AMIA Annu Symp Proc* 2007: 26-30.
22. Ash JS, Sittig DF, Poon EG, Guappone KP, Campbell EM, Dykstra RH. The extent and importance of unintended consequences related to computerized provider order entry. *J Am Med Inform Assoc* 2007; 14: 415-423.
23. Feldstein A, Simon SR, Schneider J, Krall M, Laferriere D, Smith DH, et al. How to design computerized alerts to ensure safe prescribing practices. *Joint Commission Journal on Quality and Safety*. 2004; 30: 602-613.
24. Davlong Business Solutions. Electronic medical record. Accessed at <http://www.davlong.com/electronic.html> on January 5, 2011.

25. Shoffner J, Staudt M, Marcus S, Kapp S. Using telephone reminders to increase attendance at psychiatric appointments: findings of a pilot study in rural Appalachia. *Psychiatr Serv* 2007; 58: 872-875.
26. Reda S, Makhoul S. Prompts to encourage appointment attendance for people with serious mental illness. *Cochrane Database Systematic Reviews* 2001; 2: CD002085.
27. Patel P, Forbes M, Gibson J. The reduction of broken appointments in general dental practice: an audit and intervention approach. *Prim Dent Care* 2000; 7: 141-144.
28. Lee JK, Reis V, Lui S, Conn L, Groessi EJ, Ganiats TG, et al. Improving fecal occult blood testing compliance using a mailed educational reminder. *J Gen Intern Med* 2009; 24: 1192-1197.
29. Institute of Medicine. *Crossing the quality chasm: A new health system for the 21st century*. Washington, DC: National Academy Press, 2001.