

Review Articles

Effect of health information technology interventions on lipid management in clinical practice: A systematic review of randomized controlled trials

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BACKGROUND: Large gaps in lipid treatment and medication adherence persist in high-risk outpatients in the United States. Health information technology (HIT) is being applied to close quality gaps in chronic illness care, but its utility for lipid management has not been widely studied.

OBJECTIVE: To perform a qualitative review of the impact of HIT interventions on lipid management processes of care (screening or testing; drug initiation, titration or adherence; or referrals) or clinical outcomes (percent at low density lipoprotein cholesterol goal; absolute lipid levels; absolute risk scores; or cardiac hospitalizations) in outpatients with coronary heart disease or at increased risk.

METHODS: PubMed and Google Scholar databases were searched using Medical Subject Headings related to clinical informatics and cholesterol or lipid management. English language articles that described a randomized controlled design, tested at least one HIT tool in high risk outpatients, and reported at least 1 lipid management process measure or clinical outcome, were included.

RESULTS: Thirty-four studies that enrolled 87,874 persons were identified. Study ratings, outcomes, and magnitude of effects varied widely. Twenty-three trials reported a significant positive effect from a HIT tool on lipid management, but only 14 showed evidence that HIT interventions improve clinical outcomes. There was mixed evidence that provider-level computerized decision support improves outcomes. There was more evidence in support of patient-level tools that provide connectivity to the healthcare system, as well as system-level interventions that involve database monitoring and outreach by centralized care teams.

CONCLUSION: Randomized controlled trials show wide variability in the effects of HIT on lipid management outcomes. Evidence suggests that multilevel HIT approaches that target not only providers but include patients and systems approaches will be needed to improve lipid treatment, adherence and quality. © 2013 National Lipid Association. All rights reserved.

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Achieving and maintaining statin adherence and low-density lipoprotein cholesterol (LDL-C) control in outpatients with coronary heart disease (CHD) or equivalent risk

remains surprisingly difficult, despite robust epidemiologic data that link abnormal blood lipids to CHD morbidity and mortality,¹⁻⁵ numerous randomized trials that show lipid lowering reduces CHD event rates,⁶⁻⁸ wide dissemination of evidence-based treatment guidelines,⁹⁻¹² and the establishment of LDL-C control as a quality metric.¹³ Recent data from practice surveys,¹⁴⁻¹⁶ health insurer databases,¹⁷ the National Health and Nutrition Examination Survey,¹⁸ and quality oversight groups¹⁹ show that 20% to 60% of high-risk persons fail to achieve the previously recommended LDL-C target of <100 mg/dL in clinical practice. Outcomes data show these persons experience higher event rates and incur greater health care costs.^{20,21} Nonadherence by patients and ineffective treatment by physicians contribute to suboptimal lipid control. However, in the past decade, systems barriers have been recognized as major contributors to gaps in chronic illness care,²²⁻²⁴ including for diseases such as hyperlipidemia. In response to these barriers and to rising health care costs, care delivery models better suited for disease and population management (eg, the patient-centered medical home and the more broad-based accountable care organization) and new payment models that reward care coordination and quality are being tested by the Center for Medicare and Medicaid Services and commercial payers.^{25,26} Of fundamental importance to these new care models, whether operating independently or as larger systems of care, is a health information technology (HIT) infrastructure capable of supporting population management.²⁶⁻²⁸ Under this umbrella are HIT tools that support provider decision making (through electronic risk assessment, alerts, guidelines, formularies, and prescribing), patient self-management (through risk communication, web portals, telemedicine, e-mailing, and secure messaging), and quality improvement (through registry creation, dashboards, benchmarking, outcomes reporting, and outreach support). Indeed, both large integrated health care systems, for example, Kaiser Permanente, and smaller practice settings have successfully applied one or more of these HIT tools to close lipid treatment gaps in intermediate- and high-risk patients²⁹⁻³¹ (see related article in this edition of the *Journal*). However, most of these HIT interventions have not been tested in randomized controlled trials (RCTs), making it difficult to exclude confounding variables. We therefore conducted a review of the literature for RCTs that have tested the effectiveness of HIT tools for improving lipid management and outcomes in both secondary prevention and high-risk primary prevention patients treated across the spectrum of health care delivery settings.

Methods

Data sources and searches

Medline and Google Scholar databases were searched for RCTs that have investigated the effect of HIT interventions

on the management of hyperlipidemia in ambulatory health care settings. The following Medical Subject Headings were used: Medical Informatics, including Computing Methodologies; Electronic Prescribing; Computerized Medical Records Systems and Health Records; and Dyslipidemias, including Cholesterol, LDL-C/blood; Hyperlipidemias, and Dyslipidemias. In addition to electronic searching, hand searches of bibliographies of relevant articles were conducted. Only articles published in English were included.

Study selection

Four authors (R.F., K.E.A., D.G.K., and T.A.J.) independently screened titles and abstracts from the literature search to determine study eligibility. Studies were included if they reported at least 1 lipid process measure or outcome; described the use of at least 1 electronic tool; were conducted in an ambulatory US or non-US health care setting; included patients with diabetes mellitus (DM), CHD, or at intermediate-to-high risk; and described a randomized controlled study design. An open-source web-based citation manager tool (Zotero; Center for History and News Media, George Mason University) was used to organize and display all publications for the group.

Data extraction and rating of included studies

Data were extracted independently by 3 authors (R.F., K.E.A., and D.G.K.) with the use of a spreadsheet that included study investigators, country, year of publication, years during which the study was conducted, study setting, number and characteristics of subjects, the IT user (provider, patient, system, or combination), type of IT intervention, type of control group, and outcomes. Outcomes recorded included changes in lipid process measures (eg, lipid screening or testing, lipid drug initiation, titration or adherence, or lipid referrals), or lipid outcomes (eg, percentage at LDL-C goal, absolute lipid levels, absolute risk score, or hospitalizations for CHD). Studies were rated for quality on the basis of the US Preventive Services Task Force (USPSTF) rating system, which subjectively rates assembly and maintenance of comparable groups, description of follow-up losses, intervention, measurement instruments, and described outcomes.³² In addition, studies were rated for level of evidence or effect by using the National Heart, Lung, and Blood Institute scale³³ (A = substantial, B = moderate, C = small, D = none, or ? = uncertain).

Results

Study inclusion

The search identified a total of 17,900 citations. After screening of titles and abstracts, 140 full-text studies were reviewed for eligibility, and 34 RCTs met inclusion criteria (Fig. 1).

Description of studies and interventions

Table 1 summarizes the characteristics of and interventions tested in the included studies. The 34 RCTs were published between 1998 and 2013 and were performed in the United States, Australia, Canada, Israel, The Netherlands, and Norway. A total of 87,874 outpatients were randomly assigned individually or in clusters to either intervention or control arms. Most subjects were patients in academic or community primary care clinics, including 1 study in a Kaiser Permanente primary care clinic network. However, 8 studies were performed as systems approaches, some of them removed from the point of care (POC). Subjects had type 2 DM, documented CHD or ischemic vascular disease, or elevated CHD risk on the basis of risk factors or risk scoring.

Twelve studies tested provider-level computerized decision support (CDS), including 6 with tools not part of an electronic health record (EHR) and 6 with tools embedded in an EHR. All of these tested guideline support, with or without medication support, risk calculators, alerts, computerized provider order entry (CPOE), or electronic (e-) prescribing. Ten studies assessed patient-level HIT tools, including electronic calculation of vascular age, web education or activity with or without connectivity to the health care system, telemedicine, and secure text messaging. A combination of patient and provider tools was tested in 4 studies. Eight studies investigated systems-level HIT interventions, including database monitoring by the health care system or related entities, followed by patient outreach via multiple methods, with or without primary care physician (PCP) involvement. All studies measured either a lipid process measure or clinical outcome, and 17 studies reported both. Most study durations were 12 months (range, 3–36 months). Control groups received either usual care or an unrelated intervention.

Methodological quality and effect of included studies

Study quality assessed by USPSTF criteria varied widely. Within each of the 4 categories of studies, only 3 to 4 articles were graded as good quality by the reviewers, 1 to 4 were graded as poor in quality, and the remainder were graded as fair (Figs. 2–5).

Outcomes

Provider-level HIT studies

Of the 12 randomized trials that tested provider-level HIT tools, 6 studies tested non-EHR-based CDS delivered via a personal digital assistant (PDA) or web-based tool^{34–39} (Fig. 2 and Table 1). All 6 studies tested guideline support, all but 1 study also provided medication support,³⁹ one tested an alert,³⁵ and one tested an electronic risk calculator.³⁴ Others provided additional support beyond the POC to providers (via electronic academic detailing, virtual consultation, or performance reporting) or to patients (via nursing advice).

Among these 6 trials, 4 reported either a small or moderate effect on a clinical outcome or process measure. Meigs et al³⁸ tested a web-based CDS tool with guideline and medication support vs control in 598 patients with DM and reported a small but significant increase in lipid screening and a significant 30% increase in the percentage of patients with an LDL-C <130 mg/dL in the treatment arm at 1 year (vs a 10% increase in the control group; $P = .008$.) Similarly, Cleveringa et al³⁶ randomly assigned 3291 patients with DM to CDS with guideline and medication support or control and reported a small but significant decrease in LDL-C levels (-5.8 mg/dL; data converted from mmol/L; $P < .05$ vs usual care) and in risk score at 1 year, although provider support beyond the POC

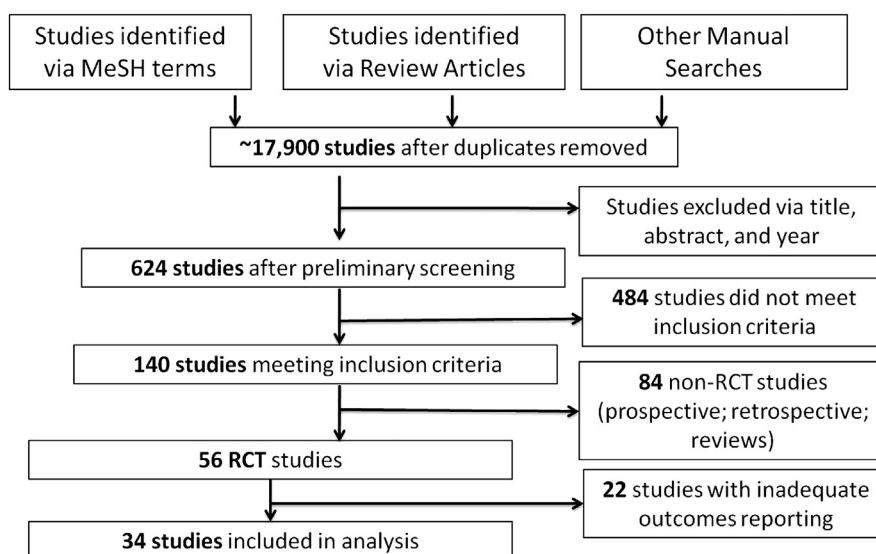


Figure 1 Flow diagram of assessed studies. MeSH, Medial Subject Heading; RCT, randomized controlled trial.

Table 1 Characteristics and outcomes of included studies

First author, year, and country of source study	Setting	Design, duration, mo	Eligibility; no. of participants	Interventions	Lipid outcomes vs control
Provider HIT interventions					
Bertoni, ³⁴ 2009, USA	Community primary care	Cluster RCT, 24	Primary prevention not on lipid therapy; 5057	CDS (via PDA): risk calculator, guidelines, medication support	Increased appropriate treatment
Smith, ³⁵ 2008, USA	Academic primary care	Cluster RCT, 30	T2DM, high CVD risk; 635	CDS (non-EHR): guidelines, medication advice, alerts, virtual consults	No effect
Cleveringa, ³⁶ 2008, Netherlands	Community primary care	Cluster RCT, 12	T2DM; 3291	CDS (non-EHR): guidelines, medication advice, reporting	Decreased LDL-C and TC at 1 y
Mehler, ³⁷ 2005, USA	Community primary care	Cluster RCT, 15	T2DM >40 y; 884	CDS (non-EHR): e-academic detailing, guidelines, medication advice	Increased screening
Meigs, ³⁸ 2003, USA	Academic primary care	Cluster RCT, 12	T2DM; 598	CDS (non-EHR): guidelines, medication support	Increased screening, increased percentage at LDL goal
Hetlevik, ³⁹ 1998, Norway	Community primary care	Cluster RCT, 18	HTN; 2239	CDS (non-EHR): guidelines	No effect
O'Connor, ⁴⁴ 2011, USA	Community primary care	Cluster RCT, 12	T2DM; 2556	CDS (via EHR): alerts, guidelines, medication support	No effect
O'Connor, ⁴³ 2009, USA	Community multispecialty	Cluster RCT, 12	T2DM; 2020	CDS (via simulated EHR): virtual patients ± KOL feedback	No effect
van Wyk, ⁴¹ 2008, Netherlands	Community primary care	Cluster RCT, 12	Primary prevention not on lipid therapy; 6163	CDS (via EHR): alerts, guidelines	Increased screening, increased treatment
Lester, ⁴⁰ 2006, USA	Academic primary care	RCT, single site, 12	CHD or equivalent; LDL-C >goal for >6 mo; 235	CDS (via EHR-email interface): guideline, medication advice, CPOE, eRx, letter	Increased treatment, increased titration, decreased LDL-C if baseline was >130 mg/dL
Sequist, ⁴² 2005, USA	Academic and community primary care	Cluster RCT, 6	T2DM and CAD; 6243	CDS (via EHR): reminders	T2DM: increased screening; CAD: increased treatment
Tierney, ⁴⁵ 2003, USA	Academic primary care	Cluster RCT, 12	Ischemic heart disease or CHF; 706	CDS (via EHR): guidelines, medication advice, CPOE, eRx	No effect
Patient HIT interventions					
Vernooij, ⁵⁰ 2012, Netherlands	Academic primary care	RCT, 12	ASVD; LDL-C > goal; 330	Web portal tailored education, e-mail to NP	Decreased risk score, decreased LDL-C
Glasgow, ⁵³ 2012, USA	Primary Care Kaiser Permanente Colorado	RCT, 12	T2DM BMI ≥ 25 and ≥1 risk factor; 463	Web portal ± phone contact ± group visit	No significant effects

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Table 1 (continued)

First author, year, and country of source study	Setting	Design, duration, mo	Eligibility; no. of participants	Interventions	Lipid outcomes vs control
Sheridan, ⁵¹ 2011, USA	Academic primary care	RCT, 3	Primary prevention at risk; 165	Web portal at POC with risk calculator; tailored education	Decreased 10-y risk score
Webster, ⁵⁴ 2010, Australia	Any adult	RCT, 21	Population-wide; 2099	Consumer Web site; treatment algorithm	No significant effects
Grant, ⁵² 2008, USA	Academic and community primary care	Cluster RCT, 12	T2DM HbA _{1c} > 7 or on Rx; 244	PHR linked to EHR	Increased treatment
Bond, ⁴⁶ 2007, USA	Academic specialty care	RCT, 6	DM >1 y and age ≥ 60 y; 124	Web portal E-messaging or online chat with nurse	Decreased TC. increased HDL-C
Grover, ⁴⁹ 2007, Canada	Community primary care	RCT, 12	CVD, DM, or at risk; 3053	Risk calculator, vascular age	Decreased LDL-C, TC; increased percentage of lipid goals
Shea, ⁴⁸ 2006, USA	Community and urban primary care	Cluster RCT, 12	T2DM ≥55 y; 1665	Telemedicine unit monitoring, Web education messaging to NP SMS to patients	Decreased LDL-C and TC
Harno, ⁴⁷ 2006, Finland	Community and academic primary care	RCT, 12	T2DM; 175	SMS to patients	Decreased TC and LDL-C
Verheijden, ⁵⁵ 2004, Canada	Academic primary care	RCT, 8	T2DM or HTN + HL; 146	Web portal nutrition counseling, messaging	No effect
Provider + patient HIT interventions					
Benner, ⁵⁹ 2008, Europe	Community primary care	Cluster RCT, 6	HBP and FHRS > 10%; 1103	CDS (PDA-based): risk calculator, heart health report	Improved LDL-C goal attainment; decrease in calculated 10-y CHD risk
Holbrook, ⁵⁷ 2009, Canada	Community primary care	Cluster RCT, 12	T2DM; 511	CDS (Web): risk tracker, alerts, guidelines, medication advice	No effect on LDL-C
Holbrook, ⁵⁸ 2011, Canada	Community primary care	Cluster RCT, 12	Primary prevention at risk; 1102	CDSS (PDA-based): risk calculator, heart age tool	Significant in subgroups only
Eaton, ⁵⁶ 2011, USA	Community and academic primary care	Cluster RCT, 12	Primary prevention; 4105	CDS (PDA-based): risk calculator, heart age tool	Significant in subgroups only
System-level HIT interventions					
Derose, ⁶⁰ 2013, USA	Kaiser Healthcare System, So. California	RCT, 12	Primary statin nonadherence; 5216	Pharmacy database monitoring and automated phone messaging	Improved statin prescription fill rates at 2 wk and 1 y
Pape, ⁶⁴ 2011, USA	Network primary care	Cluster RCT, 24	T2DM; 6963	Pharmacist outreach approved by PCP	Increased screening and treatment; decreased LDL-C; increased percentage at goals

Persell, ⁶³ 2013, USA	Academic primary care	Cluster RCT, 9	Primary prevention at risk; 435	EHR database monitoring; automated mail from PCP	Increased treatment at 9 mo and decreased LDL-C at 18 mo
Peterson, ⁶² 2008, USA	Community primary care	Cluster RCT, 24	T2DM; 7101	Non-EHR database monitoring; provider alerts; patient outreach	Improved process measures and all-or-none (HbA _{1c} , SBP, LDL-C)
Selby, ⁶¹ 2012, USA	Kaiser Permanente Northern California	Cluster RCT, 6	T2DM with CVD ± CKD; 12,582	Non-EHR database monitoring; phone outreach by non-PCPs	Decreased LDL-C at 3 mo; no effect at 6 mo
Kooy, ⁶⁵ 2013, Netherlands	Community pharmacies	RCT, 12	Secondary statin nonadherence; 1017	Pharmacy database monitoring; personal electronic reminder device	Improved statin adherence in women only
Simon, ⁶⁷ 2010, USA	Harvard Pilgrim Health Plan	Cluster RCT	T2DM; 1200	Healthplan database monitoring; automated phone outreach	No effect
Gilutz, ⁶⁶ 2009, Israel	Community primary care	Cluster RCT, 6–36	CAD; 7448	Hospital database monitoring; written provider reminders	Decreased LDL-C if >120 mg/dL; decreased hospital admissions

ASVD, arteriosclerotic vascular disease; BMI, body mass index; BP, blood pressure; CAD, coronary artery disease; CDS, clinical decision support; CDS, computerized decision support; CHD, coronary heart disease; CHF, congestive heart failure; CKD, chronic kidney disease; CPOE, computerized provider order entry; CVD, cardiovascular disease; DM, diabetes mellitus; EHR, electronic health record; eRx, electronic prescribing; FHRS, Framingham risk score; HbA_{1c}, glycosylated hemoglobin; HBP, high blood pressure; HDL-C, high-density lipoprotein cholesterol; HIT, health information technology; HL, hyperlipidemia; HTN, hypertension; KOL, key opinion leader; LDL-C, low-density lipoprotein cholesterol; NP, nurse practitioner; PCP, primary care provider; PDA, personal digital assistant; PHR, personal health record; POC, point of care; RCT, randomized controlled trial; SBP, systolic blood pressure; SMS, short message service; T2DM, type 2 diabetes mellitus; TC, total cholesterol.

PROVIDER LEVEL HIT INTERVENTIONS								OUTCOMES				STUDY BENEFIT AND QUALITY RATING	
CDS TOOLS					EHR Based	CPOE/ eRx	Other Support	Process	Clinical			Benefit	Rating
Source	Risk Calculator	Guideline Support	Medication Support	Alert/ Reminder				LDL	Risk Score	Non-LDL Clinical			
Lester ⁴⁰ 2006		X	X	x(A)	X	X		+	+	+		G	
van Wyk ⁴¹ 2008		X		x(A)	X			+				F	
Meigs ³⁸ 2003		X	X					+	+			P	
Mehler ³⁷ 2005		X	X				Academic detailing	+				F	
Cleveringa ³⁶ 2008		X	X				Report		+	+	+	F	
Sequist ⁴² 2005	X	X		X	X	X		+				P	
Bertoni ³⁴ 2009	X	X	X				Report	+				P	
Hetlevik ³⁹ 1999		X						NS	NS		NS	F	
Smith ³⁵ 2008		X	X	x(A)			Virtual Consult	NS		NS		F	
O'Connor ⁴⁴ 2011		X	X	x(A)	X				NS		NS	P	
O'Connor ⁴³ 2009		X			X		Patient Simulation		NS			F	
Tierney ⁴⁵ 2003		X	X	X	X	X		NS				G	

Figure 2 Provider-level studies: interventions, outcomes, magnitude of benefits, and ratings. A = active alert; Magnitude of benefit: ? = uncertain, gray = none, 1 blue bar = small, 2 blue bar = moderate, 3 blue bar = substantial; rating: G = good, F = fair, P = poor. HC, health care; HIT, health information technology; LDL, low-density lipoprotein; NS, non-significant; PHR, personal health record; SMS, short message service. + symbol denotes positive effects on the outcome.

(performance reporting) and patient support (nurse advice) may have influenced outcomes. Bertoni et al³⁴ randomly assigned 5057 primary prevention patients to receive lipid management via a PDA-based CDS provider tool with guideline and medication support and a risk calculator, plus a practice-level performance report, or control, finding a small but significant improvement in appropriate lipid treatment that favored the intervention (9.7% received more-appropriate lipid treatment vs control patients; $P < .01$). Mehler et al³⁷ randomly assigned 884 patients with DM older than 40 years to receive lipid management from providers who received academic detailing delivered electronically (by email and fax,) or by face-to-face contact, or who engaged in usual care, reporting a borderline increase in lipid screening by using electronic academic detailing (22.8% increase vs 11.3% increase in control groups; $P = .06$). Two studies reported no positive outcomes from non-EHR-based CDS,^{35,39} but Smith et al³⁵

hypothesized that lack of effect may have been because of a high background of care management by nurses. These data show that non-EHR-based provider-level CDS tools may have limited usefulness for improving lipid outcomes.

Six trials tested provider CDS tools embedded in or interfacing with the EHR.⁴⁰⁻⁴⁵ All 6 provided guideline support, 5 (all but O'Connor et al⁴³) used alerts, 3 provided medication support, and 1 study linked the alert to CPOE and eRx.⁴⁰ Three of the 6 trials reported a positive process or clinical outcome or both.⁴⁰⁻⁴² However, only Lester et al⁴⁰ reported a substantial change in clinical outcomes. This single-site study randomly assigned 235 patients at the provider level to usual care or to lipid management via a visit-independent secure e-mail that interfaced with the EHR and provided CDS and a link to CPOE and eRx. The investigators reported a significant increase in lipid medication prescribing at 1 month (15.3% vs 2%; $P = .001$), although this difference eroded at 1 year (24.6% vs 17.1%; $P = .14$) and

PATIENT LEVEL HIT INTERVENTIONS						OUTCOMES				STUDY BENEFIT AND QUALITY RATING	
Source	Risk/Heart Age Calculator	Web Activity w/NO Connectivity to HC system	Web Activity w/ Connectivity to HC system	Tele-Medicine/ Videoconf	Mobile/ SMS Reminder	Process	Clinical			Benefit	Rating
							LDL	Risk Score	Non-LDL Clinical		
Bond ⁴⁶ 2007			X				+		+		G
Harno ⁴⁷ 2006			X		X		+		+		F
Shea ⁴⁸ 2006				X			+		+		P
Glasgow ⁵³ 2012			X		X				NS		G
Grover ⁴⁹ 2007	X						+	+	+		G
Vernooij ⁵⁰ 2012			X			+	+	+	NS		F
Grant ⁵² 2008			X (PHR)			+	NS				F
Sheridan ⁵¹ 2011	X	X*				NS	NS	+			P
Verheijden ⁵⁵ 2004			X			NS					F
Webster ⁵⁴ 2010		X				NS					F

Figure 3 Patient-level studies: interventions, outcomes, magnitude of benefits, and ratings. Benefit: gray = none, 1 blue bar = small, 2 blue bar = moderate, 3 blue bar = substantial; rating: G = good, F = fair, P = poor. HC, health care; HIT, health information technology; LDL, low-density lipoprotein; NS, non-significant; PHR, personal health record; SMS, short message service. + symbol denotes positive effects on the outcome. *as interpreted by reviewers.

reported a significantly lower LDL-C level at 1 year in patients with levels >130 mg/dL at baseline (119 vs 138mg/dL; *P* = .04). The active, non-bypassable, e-mail alert was sent to providers once per patient, eliminating the potential of alert fatigue, a common barrier. Use rate was 99%, a number significantly higher than for other EHR-based CDS interventions. However, <40% of providers changed their prescribing as a result of the tool, citing patient factors and the opinion that the LDL-C level was close enough to goal. In addition, the generalizability of the intervention was admittedly low, given that the tool was a prototype developed within an academic clinical informatics department.

Positive process measures (either an increase in LDL-C screening or lipid medication prescribing) were reported in 2 other provider-level studies of EHR-based CDS,^{41,42} both of which also used alerts. Sequist et al⁴² randomly assigned at the provider level 6748 patients with DM or CHD to EHR-based usual care or to an EHR-based reminder system that notified the provider at the POC of care gaps and recommended conservative treatment goals, reporting a significant 1.5-fold increase in statin use at 6 months in the intervention group of patients with CHD with LDL-C ≥130 mg/dL (95% CI, 1.05–2.17; *P* = .03) and a significant 1.4-fold increase in lipid screening among patients with DM (95% CI, 1.15–

Source	PROVIDER LEVEL HIT INTERVENTIONS			PATIENT LEVEL HIT INTERVENTIONS			OUTCOMES				STUDY BENEFIT AND QUALITY RATING	
	Risk Calculator	Guideline Support	Medication Support	Risk/Heart Age calculator	Web activity with connectivity to HC system	Reminder	Process	Clinical			Benefit	Rating
								LDL	Risk Score	Non-LDL Clinical		
Benner ⁵⁹ 2008	X	X		X			+	+	+			Poor
Holbrook ⁵⁷ 2011	X	X	X		X		+	NS				Good
Holbrook ⁵⁸ 2009						X	+	NS		+		Good
Eaton ⁵⁶ 2011	X	X	X	X			NS	NS				Good

Figure 4 Provider + patient studies: interventions, outcomes, magnitude of benefits, and ratings. Benefit: ? = uncertain, gray = none, 1 blue = small, 2 blue = moderate, 3 blue = substantial. HC, health care; HIT, health information technology; LDL, low-density lipoprotein; NS, non-significant; PCP, primary care provider. + symbol denotes positive effects on the outcome.

SYSTEM LEVEL HIT INTERVENTIONS							OUTCOMES			STUDY BENEFIT AND QUALITY RATING			
	Database or Registry Monitoring and Reporting			Patient Outreach			PCP Involved	Process	Clinical			Benefit	Rating
Source	HC System	Outside Pharmacy	Health Insurer	Phone (Non-PCP)	Mail	Other Device	CDSS/ Reports		LDL	Risk Score	Non-LDL Clinical		
Derose ⁶⁰ 2013	x			X ATO				+					Good
Pape ⁶⁴ 2011	x			x			X	+	+		NS		Good
Persell ⁶³ 2003	x				x		x	+	+				Fair
Peterson ⁶² 2008	x			x			x	+	+		+		Good
Gilutz ⁶⁶ 2009	x						x	+	+		+		Good
Selby ⁶¹ 2012	x			x	x			+	NS				Fair
Kooy ⁶⁵ 2013		x				X ERD		+*				?	Fair
Simon ⁶⁷ 2010			x	X ATO				NS	NS				Poor

Figure 5 System-level studies: interventions, outcomes, magnitude of benefits, and ratings. Benefit: ? = uncertain, gray = none, 1 blue = small, 2 blue = moderate, 3 blue = substantial. ATO, automated telephone outreach; CDS, computerized decision support; ERD, electronic reminder device; HC, health care; HIT, health information technology; LDL, low-density lipoprotein; NS, non-significant. + symbol denotes positive effects on the outcome. *results positive in subset of women only.

1.72; $P < .001$). Similarly, van Wyk et al⁴¹ tested 2 types of EHR-based CDS, an alert-based tool vs an on-demand CDS tool, vs usual care in 6163 primary prevention patients, reporting that CDS linked to an alert was associated with a significant increase in lipid screening (screening rate 65% vs 35% with the on-demand tool vs 25% with usual care). Treatment was similarly improved, with the alert-based tool resulting in 66% of patients appropriately treated (vs 40% with the on-demand tool and 36% treated with usual care). After adjustment for the number of visits, practice size, and clinical factors, the alert-based tool was associated with a 1.76-fold increase in screening and 1.2-fold increase in treatment ($P < .05$).

Together these data suggest that EHR-based provider-level CDS tools that offer guideline and medication support, with or without alerts, may be effective for improving lipid process measures and clinical outcomes in practice. However, several investigators noted barriers to their implementation. Negative physician attitudes toward treatment guidelines were reported in 3 studies and were identified by Tierney et al⁴⁵ as the main reason for a null effect. A few studies attempted to overcome this barrier by providing a range of treatment goals,⁴⁰ having participants co-develop workflow integration⁴² and setting recommendations to conservative, less-controversial thresholds.⁴² Alert fatigue was also another common barrier, and preventive measures such as reducing alert frequency and providing succinct messages were attempted. The inclusion of active alerts

generated mixed results. Although positive outcomes with the use of active alerts were observed by Lester et al⁴⁰ and van Wyk et al,⁴¹ neither Smith et al³⁵ nor O'Connor et al⁴⁴ observed a benefit, although a high background of lipid treatment in the latter study may have limited the ability to detect between-group differences.

Patient-level HIT studies

The 10 trials that tested patient-level HIT tools (Fig. 3 and Table 1) investigated the effects of electronic risk calculators, web-based education and monitoring (with or without connectivity to the health care system), tele-video-conferencing, or mobile technologies. Six of the 10 studies reported improved clinical outcomes (lowered lipids or lower risk scores or both) or process measures,⁴⁶⁻⁵¹ and 1 study⁵² reported a positive effect on process measures only. Several tested patient HIT tools that allowed connectivity to the health care system. Among these, Bond et al⁴⁶ randomly assigned 62 patients with DM or age >60 years treated at a single site to usual care or use of an interactive patient web portal, with connectivity to a study nurse via asynchronous communication (eg, e-mails and a bulletin board) as well as synchronous communication (eg, instant messaging and chat), along with other educational materials and weekly group sessions, achieving small but significant improvements in total cholesterol (165 vs 170 mg/dL at baseline; $P < .05$), high-density lipoprotein cholesterol (50 vs 44 mg/dL at baseline; $P < .05$) vs control patients.

Harno et al⁴⁷ randomly assigned 175 patients with DM treated at multiple sites to usual care or to use of a web portal with connectivity to care managers with access to the patient's web-based data, plus short message service text messaging, to track and target multiple risk factors, reporting small but significant reductions in total cholesterol (183 vs 191 mg/dL; $P < .05$; values converted from mmol/L to mg/dL), and LDL-C (97.5 vs 104 mg/dL) and fewer face-to-face visits. Shea et al⁴⁸ randomly assigned 1665 patients with diabetes older than 55 years to usual care or use of a patient home telemedicine program with a web portal, video conferencing, secure messaging, and EHR interface, plus case managers and physicians to track and treat risk factors, reporting a small but significant decrease in LDL-C levels of 9.5 mg/dL ($P < .001$) in the intervention group at 1 year.

Smaller but significant effects on outcomes were reported in 3 other studies that provided patients with electronic connectivity to health care providers. Grant et al⁵² tested a personal health record with connectivity to the provider EHR, which allowed 244 patients with DM to review lipid test results and to message their providers in between visits, reporting an increase in lipid medication prescribing compared with usual care (11% vs 0%; $P = .03$) and a nonsignificant decrease in LDL-C at study end. Vernooij et al⁵⁰ randomly assigned 330 high-risk patients (with documented coronary, cerebral, or peripheral arterial disease and at least 2 risk factors not at goal) to an interactive web portal that delivered color-coded risk factor reports, treatment goals, nurse advice, a correspondence history between the nurse and patient, risk-factor news, and a tracking tool, reporting small but significant relative reductions in Framingham risk scores of -12% , a decrease in LDL-C levels of 11.6 mg/dL (converted from mmol/L; $P < .001$), and lower rates of tobacco use (-7.7%) in the intervention arm at 1 year. One study that tested a patient-level HIT tool with connectivity to the health care system showed only marginal changes in lipid-related outcomes. Glasgow et al⁵³ randomly assigned 463 patients with DM and at least 1 other vascular risk factor to usual care in a Kaiser Permanente primary care network or to use of a bilingual, web-based DM self-management program with or without human support to target adherence to diet, lifestyle, and medications, reporting significant improvements in behavioral outcomes but nonsignificant improvements in biological outcomes, possibly because of the high background of DM care management. Two studies that tested patient web-based education with no connectivity to the health care system showed no effects on outcomes.^{54,55}

Two patient-level studies tested the utility of communicating vascular risk/vascular age to patients.^{45,47} Grover et al⁴⁹ randomly assigned 3053 patients with DM, cardiovascular disease, or at high risk to receive usual care with or without a computer-generated cardiovascular risk profile with calculation of vascular age provided quarterly for 12 months, showing a small but significant decrease in LDL-C vs control (-3.3 mg/dL) and an increase in the

likelihood of reaching lipid targets (odds ratio [OR], 1.2; 95% CI, 1.07–1.48), with the greatest effect in high-risk persons. Sheridan et al⁵¹ tested the effects in 165 high-risk primary prevention patients of a self-directed web-based risk calculator with tailored education delivered in the clinic setting and in follow-up mailings, reporting a 25% increase in self-reported medication adherence ($P < .05$) and a small decrease in risk scores in the intervention group at 3 months. Analyses to confirm self-reported adherence to cholesterol medication found a significant reduction in total cholesterol (-45.6 mg/dL; $P < .05$) but only among those reporting increased adherence.

Taken together, these data suggest that patient-level HIT tools, especially those that allow connectivity to a health care provider or that communicate vascular risk or vascular age, may provide practices with additional leverage for improving lipid control, although their effects over longer follow-up periods remain untested.

Provider plus patient HIT studies

Four randomized trials tested a combination of provider and patient HIT tools used together, with small and mixed results^{56–59} (Fig. 4 and Table 1). All studies combined provider-level CDS (risk calculators, guideline support, medication support, and laboratory data) with patient-level tools (calculation and communication of vascular age, web activity with connectivity to the health care system, or reminder messages). Only Benner et al⁵⁹ reported a small improvement in clinical outcomes by using the combination of a provider-level non-EHR-based risk calculator and patient-level heart health report in 1103 high-risk primary prevention patients, reporting a relative decrease in risk score of 25.7% in the intervention group (vs 18.2% in the usual care group), small decreases in LDL-C cholesterol (from 150 mg/dL to 131 mg/dL in the intervention group and to 135 mg/dL in the usual care group; $P = .052$) and in LDL-C goal attainment (OR of 1.6 that favored the intervention; $P = .005$). A similar study by Eaton et al,⁵⁶ which tested the utility of a provider-level PDA-based CDS tool and patient-level risk calculator and vascular age tool in high-risk primary prevention patients, reported no difference in clinical outcomes over usual care, although a high background of lipid treatment in practices at baseline, and other factors, may have made it difficult to detect between-group differences. Two other patient-plus-provider-level HIT studies showed an improvement in process measures (lipid treatment intensification) only.^{57,58} Holbrook et al⁵⁸ tested the effect of a shared web-based DM risk tracking tool that interfaced both with the provider EHR and with the patient via a web portal and an automated telephone outreach (ATO) reminder system, reporting improvement in a composite score for DM care but no significant effect on LDL-C control, possibly because of technical barriers. Holbrook et al⁵⁷ tested an improved shared DM risk tracking tool with more CDS for an extended follow-up period, again, reporting only improved process but not clinical outcomes, and, again, suggesting that technical barriers, for both patients

and providers, may have negatively affected outcomes. Taken together, these studies show that provider and patient-level HIT tools used together but without systems-level support, and when not directly imbedded in the EHR, may have limited utility.

System-level HIT studies

Eight trials evaluated system-level HIT interventions on population management of hyperlipidemia, 2 studies conducted within Kaiser Permanente regional networks,^{60,61} 3 studies within large primary care networks in the United States,^{62–64} one each in a non-US pharmacy⁶⁵ or hospital network,⁶⁶ and one by a US health insurer⁶⁷ (Fig. 5 and Table 1). All involved monitoring by non-physicians of EHR-based registries or other clinical databases for quality gaps, followed by patient outreach via email, phone, mail, or an electronic device, with or without PCP involvement or PCP reports. Four of the 8 trials reported a positive clinical outcome,^{62–64,66} and 7 reported a positive effect on a process measure.^{62,60,61,63–66} One of the most substantial effects was from a centralized pharmacist intervention by Derose et al,⁶⁰ who monitored the Kaiser Permanente Southern California pharmacy database for primary statin nonadherence and randomly assigned 5216 nonadherent patients to ATO and mail reminders vs usual care, reporting a significant increase in statin prescription fill rates at 2 weeks and at 1 year in the intervention arm (combined statin dispensing rate 42% in the intervention arm vs 26% in control patients; $P < .001$). The ATO message provided in Spanish to patients with Spanish as their first language led to significant improvements in fill rates, suggesting that language barriers at the POC may play significant roles in primary nonadherence. Another substantial effect on lipid process measures and outcomes by a systems intervention that involved centrally located pharmacists was reported by Pape et al,⁶⁴ who randomly assigned 6963 patients with DM in 9 clinics (in a 2:1 design) to lipid management via a web-based care management tool (with CDS, quality reporting, benchmarking, and automated patient outreach) or to the same database tool with pharmacist-led monitoring, medication management, and outreach (with PCP approval), reporting significant increases in lipid testing, statin prescribing (15% higher likelihood; $P = .008$), and in the percentage of patients at LDL-C goals (78% vs 50%; $P = .003$) in the intervention arm at 2 years. The study demonstrated that the utility of multifaceted HIT interventions is enhanced significantly by team-based care. Others however, showed that systemwide team-based care protocols may not be enhanced further by alerts and may be difficult to change. Selby et al⁶¹ randomly assigned 12,582 high-risk patients receiving care management in the Kaiser Permanente/Northern California Prevent Heart Attacks and Strokes Everyday (PHASE) cardiovascular risk registry to usual database monitoring and outreach vs database monitoring and outreach enhanced with electronic priority flags to identify patients in need of treatment intensification, reporting only a small change in lipid treatment

intensification rates at 3 months only and no significant change in LDL-C at 3 months or 1 year. The investigators attributed the marginal benefits to incomplete care manager outreach to flagged patients mostly because of difficulty incorporating the intervention into the already established protocols, as well as to a high background of risk factor control in both groups. Peterson et al⁶² reported improved lipid-related outcomes from systematic team-based DM care in 7101 patients treated in 24 primary care clinics in a family practice research network who were randomly assigned at the practice level to care guided by a clinical information system that provided database monitoring, phone outreach, and provider alerts and reports, with support from physician champions and care coordinators, or to usual care. At 12 months, patients in the intervention arm demonstrated a significant 8.6% increase in LDL-C testing ($P < .001$) and a significant increase in the achievement of a composite of lipid, blood pressure, and glycemic control (12.6% increase in the intervention arm vs 8.5% in control patients; $P < .001$). Two other investigators reported results suggesting that systems interventions for improving lipid management can produce outcomes even when team care resources are limited, but that longer follow-up may be required to show their effects. In a small systemwide quality improvement project in a single academic primary care site, Persell et al⁶³ monitored an EHR database for lipid treatment and adherence gaps and, randomly assigned 435 patients to receive usual care or a one-time automated mail message (approved and signed by the PCP) communicating cardiovascular risk and how lipid therapy might reduce this risk, and reported a significant increase in statin prescriptions in the intervention group at 9 months (11.9% vs 6%; OR, 2.1; 95% CI, 1.05–4.32; $P = .038$). However, it took extended follow-up to 18 months to report a significant decrease in LDL-C levels of at least 30 mg/dL in the intervention vs control groups (22.5% vs 16.1%; OR, 1.6; 95% CI, 1.05–2.4; $P = .029$). Gilutz et al⁶⁶ monitored an integrated health care system database for patient's cardiovascular diagnoses, lipid levels, and lipid medication use and randomly assigned 7748 patients to receive usual PCP care or PCP care guided by simple written reminders that contained conservative recommendations, including referral to a metabolic clinic for nonadherent patients. After 36 months of follow-up, a small but significant increase in lipid medication prescribing was observed for patients in the intervention arm (59% vs 53.7%; $P < .003$), and a small but significant proportional decrease in LDL-C levels was observed in patients with baseline values >120 mg/dL randomly assigned to the intervention (to 121.9 mg/dL, a 16.2% reduction vs to 124.3 mg/dL, a 14.8% reduction, for control patients). A small decrease in the rate of cardiac rehospitalizations was also reported among patients adequately treated with lipid drugs vs patients who were not (37% vs 40.9%; $P < .001$), although no details about admission diagnoses were provided. In contrast to these population management approaches performed within health care systems, 2 investigators reported null effects from

similar approaches performed outside of the realm of the health provider.^{65,67} Simon et al⁶⁷ at Harvard Pilgrim Health Plan monitored the health insurers' database to identify patients with diabetes with poor control and randomly assigned 1200 patients to receive usual care vs automated telephone outreach and found no change in lipid control or any other measure at 1 year. Kooy et al⁶⁵ monitored an independent pharmacy network database in The Netherlands for statin nonadherence and randomly assigned 1107 patients to receive an electronic reminder device vs usual care, reporting no difference in outcomes in the intervention group as a whole, although results in women were positive.

Overall, the data suggest that system-level HIT interventions, whether applied in large integrated health care systems, medium-sized practice networks, or single-practice sites, can facilitate population management of hyperlipidemia and can close quality gaps, sometimes substantially, and outcomes may be enhanced by care manager support of PCPs, but simpler interventions performed over longer periods can also produce change.

Discussion

This is believed to be the first systematic review of RCTs which have tested the effect of HIT interventions specifically on lipid management processes of care and clinical outcomes in high- and intermediate-risk patients. This review of 34 RCTs with 87,874 patients found wide variability in the clinical utility of HIT interventions delivered at the provider, patient, and systems level for closing lipid quality gaps. However, 23 of the 34 studies reported some improvement in a process measure or clinical outcome. Qualitatively, the data in aggregate suggest mixed benefit from provider-level CDS tools, probable benefit from patient-level HIT tools that allow connectivity to health care providers and which communicate vascular risk or vascular age, and potentially large benefits from systems-level HIT interventions that involve database monitoring and patient outreach by any method, especially by centralized care team members, with added value when PCP messages are incorporated. The latter 2 categories of HIT interventions are especially crucial for population management, because provider-level HIT interventions are usually (although not always) visit dependent, whereas systems-level and patient tools have the capacity to reach patients between visits and when lost to follow-up.²⁵

Despite these positive findings, this review found that only 14 of the 34 studies analyzed showed any improvement in clinical outcomes, that is, reduction in lipid levels, predicted risk, or actual risk. Provider-level CDS tools in particular reported mixed results. The investigators suspect this may be due, in part, to the use of non-EHR-based tools in older studies, resistance to guideline-based care in some health care delivery settings, difficulty incorporating changes in provider workflows at the POC and, as Lester et al⁴⁰ suggested, failure to link provider alerts to action

tools. However, the investigators also suspect that inability to detect between-group differences in many studies may have been due to design flaws, including a high background of lipid treatment in many of the study settings, temporal trends toward more intensive lipid treatment during the time frame in which many were performed, underutilization of interventions by many providers randomized to active arms, insufficient numbers and heterogeneity of subjects, and short durations of follow-up. The latter point deserves emphasis. Most studies measured outcomes during 12 months only (and one at just 3 months), and the time frame for reporting improved lipid levels from an intervention, especially in primary prevention patients who may have a history of nonadherence, is likely much longer. Indeed, it should be noted that in large integrated health care systems, substantive improvements in outcomes from disease and population management of hyperlipidemia are typically achieved over years.^{68,69}

Some of these findings are similar to, although some diverge from, other reviews of the impact of HIT on care quality. For provider-level HIT tools, similar to the present study, Souza et al⁷⁰ reviewed 41 RCTs that used CDS for improving preventive health outcomes and found CDS improved primarily processes of care but not clinical outcomes. Likewise, McKibbin et al⁷¹ reviewed 87 RCTs that used CDS and CPOE tools in inpatients and outpatients and found almost half of the studies reported improved processes of care, but few reported improved clinical outcomes. In contrast to these findings, in a review of 162 RCTs that tested specific CDS elements, Rosanov et al^{72,73} found active provider alerts to be superior to passive alerts for improving outcomes. However, of the 4 studies reviewed herein which used active alerts, only 1 reported an improvement in clinical outcomes. Unlike the findings of this review, Rosanov et al⁷² also reported a low effect from provider HIT interventions linked to CPOE. However, the 1 study reviewed herein that linked CDS to CPOE produced substantial effects on processes of care and clinical outcomes, although several strategies were used to mitigate alert fatigue, likely improving the utility of the tool. For patient-specific interventions, the findings of the present review are similar to those of Ammenworth et al⁷⁴ and Cutrona et al,⁷⁵ whose analyses found that patient portals and reminder systems improve adherence. Finally, for systems-level HIT interventions, the findings of this study are aligned with those of Cutrona et al⁷⁵ who found significant evidence in support of automated, electronic outreach for improving cardiovascular medication adherence.

This review of the literature has some limitations. First, the rapid evolution and lack of uniformity related to HIT terminology and taxonomy may have affected the ability to conduct a complete and up-to-date search with the use of available Medical Subject Headings terms. Second, study limitations were significant, as discussed earlier, which likely affected individual outcomes and the conclusions we were able to draw. Third, the fact that many interventions were multifaceted made it difficult to isolate and analyze

the primary tool being tested in some trials. Fourth, categorization of HIT interventions into provider-, patient-, and systems-level tools was pragmatic, but some studies were difficult to categorize because the end users overlapped, and the number of studies within each category was relatively small. Finally, limiting the analyses to RCTs obviously excluded many well-designed prospective demonstration projects that have shown the effectiveness of other interventions for improving lipid outcomes.

However, the strengths of this review include the fact that a large body of literature was scanned via several methods, uniform inclusion criteria were applied, and studies from a wide spectrum of US and non-US health care settings were included. We also included all currently known HIT tools, categorized them in a clinically relevant way, and analyzed their effects on the entire spectrum of process measures and clinical outcomes related to lipid management. Finally, validated scoring tools were used to rate study quality and the magnitude of their effects.

Conclusion

In conclusion, this review of RCTs of HIT interventions for improving lipid outcomes suggests a wide variety of tools can be applied across a broad spectrum of practice settings, and benefits may begin to accrue in relatively short periods of time, especially in practices with low rates of lipid treatment, medication adherence and LDL-C control at baseline. However, the magnitude of these benefits varies widely, from small changes in process measures to substantial changes in clinical outcomes, although some data suggest that longer follow-up may lead to more significant and sustained effects. There is also some suggestion from the findings that the magnitude of benefits from HIT tools may vary by the end user. In particular, the authors of this review found interventions that connect patients to the health care system may be able to provide practices with untapped leverage for improving lipid medication adherence and LDL-C control, and these interventions appear to hold promise for making lipid management truly patient centered, and for transforming disease prevention in general.⁷⁶ In addition, the data suggest system-level HIT tools that facilitate quality reporting, benchmarking, and patient outreach by care teams, either through EHR-based registries or relational databases, have the potential to provide practices of all sizes with the kind of systems approaches for closing lipid treatment and adherence gaps previously available only in large integrated health care delivery systems. Such visit-independent tools are fundamental to population management and will be crucial for practices if and when delivery and payment models transition to accountable, value-based care. However, this review and those of others have found that provider-level CDS tools may have limited benefit for improving lipid outcomes at the present time, possibly because they are traditionally visit dependent and are often viewed negatively by providers. The authors

estimate this may improve as providers become more incentivized to close treatment gaps and as practices learn how best to incorporate provider tools into workflows or to make some of them visit independent. Indeed, these data suggest much more research is needed, including in the areas of HIT functionality and performance, and usage behavior and satisfaction,⁷⁷ before the maximum benefits on care quality and productivity are realized.

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