Risk Reduction to Disease Management: Clinical Pharmacists as Cardiovascular Care Providers

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Abstract: Most cardiovascular diseases are caused by modifiable risk factors yet prevalence continues to increase and heart disease remains the leading cause of death in the United States. Screening, identifying and appropriately managing high risk patients are strategies to shift the paradigm from treatment to prevention. Pharmacists are an underutilized population health resource despite robust evidence to support their roles as interdisciplinary team members and direct patient care providers in both inpatient and outpatient settings. This article aims to highlight the multifaceted function and impact of clinical pharmacists on cardiovascular risk reduction and disease management. (Curr Probl Cardiol 2019;44:276–293.)

Cardiovascular disease (CVD) is the leading cause of morbidity and mortality in adults worldwide. It is estimated that by 2035 > 130 million adults within the United States will have some form of CVD which is further burdened by the aging population.[1] The concept of cardiovascular health, along with the 2020 goal to improve cardiovascular health by 20% while reducing death from CVDs and stroke by 20%, was introduced by the American Heart Association in 2011.[1] Characterized by 7 metrics, containing both health behaviors (diet quality, physical activity, smoking, body mass index) and health factors (blood cholesterol, blood pressure, blood glucose), there is an expanded focus on prevention in addition to the treatment of established CVD. Yet

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the identification and control of modifiable risk factors, along with adherence to clinical practice guidelines, remains suboptimal.

Team-based care as a means to addressing the developing CVD epidemic is endorsed by the American College of Cardiology.[2,3] Pharmacists are accessible providers and interact with patients at multiple touch points from inpatient to outpatient settings and finally within the community. Advanced training, through postgraduate residency, fellowship, multidisciplinary credentialing, and board certification, distinguish clinical pharmacists and clinical pharmacy services (CPS). Defined as "a health sciences discipline in which pharmacists provide patient care that optimizes education, therapy and promotes health, wellness and disease prevention"[4] CPS comprises complex medication management, through collaborative practice with a physician or as an independent pharmacist provider, transitional care focused on preventing medication errors and patient education. Therefore, clinical pharmacist interventions have extensively demonstrated a positive impact on 3 major domains: therapeutic, safety, and humanistic outcomes.[5]

Specialized clinical training explicitly in cardiology is available as a second-year postgraduate year pharmacy residency. After completion of this residency, or with significant practice experience dedicated to cardiology, a pharmacist is eligible for cardiology board certification by examination. The delivery of cardiovascular care to patients by a clinical pharmacist can occur within primary care offices, institutional settings, cardiology practices, community pharmacies, and managed care organizations. CPS embedded in primary care or a patient-centered medical home traditionally focus on modification of risk factors, such as diabetes, smoking, hypertension, obesity and dyslipidemia, and prevention of CVD. At institutional settings, cardiology pharmacists frequently round in the coronary care unit and are involved treatment of acute CVDs such as stroke and cardiac arrest. Management of chronic CVDs, such as heart failure, or longitudinal anticoagulation monitoring can also be performed by pharmacists practicing in primary care or cardiology clinics. Though the exact role may vary by setting, a pharmacist's extensive drug knowledge results in a patient-centered approach to pharmacotherapy. This paper will highlight clinical pharmacists as cardiovascular care providers from risk reduction to disease management across the continuum of care.

Risk Reduction

Diabetes

In 2017, the Centers for Disease Control and Prevention reported that over 100 million adults are living with diabetes or prediabetes.[6] The

TABLE 1. Metabolic effects and cardiovascular outcomes of commonly used antihyperglycemics. Adapted from reference[79]

Drug class	Metabolic effects	Impact on cardiovascular outcomes
Insulin	Weight gain	Neutral
Biguanides	Weight loss	Metformin: decreased risk
Sulfonylureas	Weight gain	Neutral
Thiazolidinediones	Weight gain	Pioglitazone: potential benefit but increased risk of HF
Glucagon-like peptide-1 receptor (GLP-1) agonists	Weight loss	Exenatide: neutral Liraglutide: FDA-approved to reduce heart attack, stroke, and CV death in patients with T2DM and established CVD Lixisenatide: neutral Semaglutide: decreased risk
Dipeptidyl peptidase-4 (DPP4) inhibitors	Weight neutral	Alogliptin: increased risk of HF Linagliptin: increased risk of HF Saxagliptin: increased risk of HF Sitagliptin: neutral
Sodium-glucose co-transporter 2 (SGLT2) inhibitors	Weight loss BP reduction TG reduction	Canagliflozin: decreased risk Empaglizoin: FDA-approved to reduce risk of CV death in patients with T2DM and established CVD

BP, blood pressure; CV, cardiovascular; CVD, cardiovascular disease; FDA, Food and Drug Administration; HF, heart failure; TG, triglycerides; T2DM, type 2 diabetes mellitus.

burden of diabetes is disproportionate as prevalence varies significantly by ethnicity, education level, socioeconomic status, and geographical region.[7] It is estimated that only 52.5% of patients achieve a target hemoglobin A1c of <7%.[8] Consequently, many patients carry a substantial risk to develop cardiovascular complications such as coronary heart disease, stroke, peripheral artery disease, and cardiomyopathy.

The provision of diabetes care is complex and requires consistent follow-up, patient-tailored education and motivation. The role of a clinical pharmacist includes prescribing antihyperglycemics, insulin titration, longitudinal blood glucose monitoring, and counseling through standardized diabetes self-management education. Such pharmacist interventions are well documented to increase medication adherence, improve glycemic control, and reduce cardiovascular risk.[9-12] In a meta-analysis of 7417 patients conducted by Fazel et al., hemoglobin A1c improved by 1.1% ($P < 0.05$) in diabetic patients managed by pharmacists compared to practices with no pharmacist involvement.[13] Furthermore, with the myriad of available insulins and diabetic supplies such as continuous blood glucose monitors and insulin pumps, incorporating a pharmacist as part of a patient's health care team can improve access while reducing health care costs.[14]

TABLE 2. Clinical pharmacist impact on acute stroke treatment

Study	# Patients evaluated	DTN < 60 minutes	DTN < 45 minutes	Overall DTN time reduction
Montgomery K, et al. 2015[44]	38—Pharm	71%	42%	20 minutes
	59—No pharm	39%	19%	(95% CI: 6.6-33.4)
Gosser RA, et al. 2016[45]	67—Pharm	30%	NR	20 minutes
	38—No pharm	16%		(69.5 vs 89.5 minutes; $P = 0.0027$)
Rech MA, et al. 2017[46]	45—Pharm	71%	NR	25 minutes
	80—No pharm	29%		(48 vs 73 minutes; $P < 0.01$))
Jacoby JS, et al. 2018[47]	49—Pharm	71%	49%	12 minutes
	51—No pharm	61%	25%	(46 vs 58 minutes; $P = 0.019$)

DTN, door-to-needle; NR, not reported; Pharm, pharmacist.

Antihyperglycemic pharmacotherapy can be difficult to choose after initiation of first-line metformin since there are multiple adjunct medications that can be used when factoring patient-specific preferences and comorbidities. Generally, pharmacists modify regimens based on a drug's hemoglobin A1c lowering potential, hypoglycemia risk, cost, and weight effects. However increasing evidence from cardiovascular outcomes studies now favor certain drug classes, such as glucagon-like peptide-1 receptor agonists or sodium-glucose co-transporter 2 inhibitors, to lower cardiovascular risk.Table 2 summarizes commonly prescribed antihyperglycemics from this perspective. As cardiologists may not be familiar or comfortable prescribing these newer agents, clinical pharmacists can be instrumental in appropriate drug selection to mitigate risk and maximize outcomes.

Smoking Cessation

Tobacco use is the largest preventable cause of premature death in the United States. In 2016, 37.8 million adults were active cigarette smokers with 76.1% reporting daily use.[15] Smoking is a major modifiable risk factor for CVD and specifically is a cause of coronary heart disease, stroke, and peripheral vascular disease.[16] Smoking cessation benefits patients at any age and approximately 68% of adult smokers express the desire to quit.[17] 6-month quit rates vary by smoking cessation pharmacotherapy

agent and range from 19.0% (nicotine replacement gum) to 33.2% (varenicline) and 36.5 % (combination nicotine replacement therapy).

Clinical pharmacists are able to provide behavioral support and as drug experts are particularly poised for medication management. Augustine et al. retrospectively reviewed long-term quit rates of smokers participating in a medication management clinic where pharmacists provided pharmacotherapy and telephonic smoking cessation counseling.[18] Upon enrollment, the pharmacist reviewed treatment options, such as varenicline, nicotine replacement or bupropion, along with side effects and administration to help guide the patient in selecting a smoking cessation aid. Subsequent telephonic monitoring was determined by therapeutic product and was based on anticipated dose titration or potential for an adverse drug event. Of the 238 patients enrolled, 51 patients (21%) completed the smoking cessation program and were smoke free for 30 days. From the group that completed the program 35% and 24% had successfully quit smoking at 7-month follow-up and 13-month follow-up, respectively.

Hypertension

The prevalence of hypertension in the U.S. among adults aged ≥20 years is estimated to be 34%, equating to 85.7 million affected individuals. Despite focus and efforts, the attributable death rate has increased 10.5% during the 2005—2015 time frame.[1] The role of the pharmacist is well established and encompasses medication management, disease state education, and patient counseling.[19] Involvement of a clinical pharmacist has been shown improve control of this CV risk factor across a variety of settings and patient populations.

The prospective, randomized controlled RxACTION trial assessed the impact of pharmacist care on BP management through community pharmacies, primary care clinics, and hospital outpatient clinics. Pharmacists evaluated and educated patients on CV risks, reviewed antihypertensive regimens and prescribed or titrated medications according to national guidelines. At the 6-month treatment follow-up, pharmacist care provided an additional 6.6 mm Hg reduction in systolic blood pressure ($P < 0.0006$) and 3.2 mm Hg reduction in diastolic blood pressure ($P < 0.01$) compared to usual care.[20] Hirsch et al. also noted similar results in a collaborative physician-pharmacist medication therapy management clinic; patients receiving pharmacist care had a 7.1 mm Hg reduction in mean systolic blood pressure while conversely patients in the usual care group had a 1.6 mm Hg increase ($P = 0.008$). Additionally, a greater percentage of

patients achieved blood pressure goals in the pharmacist cohort compared to usual care, 81% vs 44% ($P < 0.001$), respectively, at 6 months.[21]

Pharmacist-driven hypertension management in complex patients, such as those with chronic kidney disease or treatment-resistant hypertension, has also yielded positive results.[22]

In addition to collaborative care, other pharmacist interventions resulting in blood pressure improvement consist of 24-hour blood pressure monitoring, motivational interviewing, disease state education, telemedicine, and refill reminders.[23,24]

Weight Loss

Obesity rates have steadily increased over the last 20 years and in 2015-2016 the prevalence of obesity among U.S. adults was 39.8%.[25] Adults who are overweight have an increased risk for CVD, particularly coronary heart disease.[26] Counseling for lifestyle changes improves CVD risk factors and reduces the incidence of type 2 diabetes.[27] Furthermore, intensive behavioral counseling in overweight patients with hypertension, dyslipidemia, impaired fasting glucose, or metabolic syndrome is recommended by the U.S. Preventive Services Task Force. Pharmacists, particularly in the community setting, can provide such counseling. Therapeutic lifestyle changes, including weight loss, are also structured into patient education in clinical pharmacist-driven diabetes and hypertension management.[10,28]

There are limited data on the effectiveness of pharmacist-driven weight management clinics. However, adoption of newer weight management medications, such as phentermine/topiramate or lorcaserin, into clinical practice is poor as evidenced by low prescribing rates.[29] Lorcaserin may be particularly beneficial in patients with high cardiovascular risk as it has been associated with a number of beneficial cardiometabolic improvements, such as blood pressure, heart rate, low density lipoproteins, high density lipoproteins, and triglycerides,[30] with upcoming long-term cardiovascular safety data.[31] The Veterans Health Administration has identified that pharmacists should be involved in the collaborative effort to prescribe adjunctive pharmacotherapy as part of a patient's weight loss program.[32]

Dyslipidemia

Low-density lipoprotein cholesterol (LDL-C) is a risk factor for CVD incidence, recurrence, and fatal outcome. Reduction from baseline is an important marker as even a 1% reduction in LCL-C decreases CVD risk

by 1%.[33] Multiple studies have determined that pharmacist-driven dyslipidemia management results in a greater reduction in LDL-C when compared to other health care providers on an interdisciplinary team.[34-36] Specifically, Tsuyuki et al. demonstrated that pharmacist-driven dyslipidemia management resulted in a 3-fold increase in patients who achieved target LDL-C goals compared to the standard of care in the community pharmacy setting.[37]

Statins are the cornerstone of dyslipidemia treatment however real-world utilization for both primary and secondary prevention of atherosclerotic cardiovascular disease is suboptimal.[38,39] Patients who would benefit from a statin pharmacotherapy based on clinical practice guidelines are often identified during a comprehensive visit with a clinical pharmacist. As statin intolerance may be an issue for some patients, a pharmacist's drug knowledge can lead to alternatives, such as lowering a statin dose, changing a statin to avoid drug-drug interactions, or selecting a statin with desirable pharmacokinetics, to avoid discontinuation of therapy.

However, statin-treated patients still have residual risk for CVD. In addition to powerful LDL-C lowering effects, either as monotherapy or adjunct to statin therapy, proprotein convertase subtilisin/kexin type 9 inhibitors are increasingly exhibiting mortality benefits in outcomes trials.[40,41] Administered every 2-4 weeks by subcutaneous injection, drug cost limits the use of PCKS9 inhibitors as insurance companies require special claims processing or prior authorization. One potential strategy to facilitate drug obtainment is to involve a clinical pharmacist as evidenced in a proof of concept study which utilized an electronic medical record consult service to screen for therapeutic appropriateness and collaborate with specialty pharmacies.[42]

Acute Care

Embedding a clinical pharmacist within the cardiovascular care team at institutional setting results in a reduction of medication errors,[43] adverse drug events[44] and improved outcomes.

Management of acute ischemic stroke with recombinant tissue plasminogen activator is highly time-sensitive and several studies have demonstrated that pharmacists dedicated to acute stroke management can improve hospital performance in door-to-needle time. Pharmacist roles included calculating and preparing appropriate doses, assessing for contraindications, educating family members on risks and benefits of recombinant tissue plasminogen activator and assisting in management of

TABLE 3. Cardiovascular drug-related problems and clinical pharmacist interventions adapted from reference[78]

Drug-Related Problem	Description	Example	Intervention
Untreated indications	Patient has an indication that requires drug therapy but is not receiving any drug for that indication	Patient without contraindications not prescribed high-intensity statin during hospitalization for AMI	Disease-state focused medication reconciliation and atorvastatin 80 mg prescribed at discharge
Improper drug selection	Patient is prescribed the wrong drug for stated indication	Patient with HFrEF prescribed metoprolol tartrate	Conversion to evidence-based beta-blocker metoprolol succinate
Subtherapeutic dosage	Patient is being treated with too little of the correct drug for their medical problem	Apixaban dosed 2.5 mg twice a day in an elderly woman with normal renal function	Therapeutic dose adjustment to 5 mg twice a day for appropriate VTE prevention
Failure to receive drugs	Patient has a medical problem resulting from not receiving a drug (eg, for pharmaceutical, psychologic, sociologic, or economic reason)	Patient prescribed ticagrelor after PCI but unable to start therapy as an outpatient due to excessive drug copay cost resulting in stent thrombosis	Alternate cost-effective antiplatelet identified and prescribed prior to discharge
Supratherapeutic dosage	Patient is being treated with too much of the correct drug	Elderly patient with CKD initiated on digoxin 0.25mg daily for HFrEF and atrial fibrillation resulting in trough serum concentration of 2.2 ng/mL	Geriatric and renal dose adjustment to avoid drug toxicity
Adverse drug reactions	Patient has a medical problem resulting from an adverse drug event	Peripheral edema in a hypertensive patient receiving high dose amlodipine	Calcium channel blocker discontinued and alternate antihypertensive initiated

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TABLE 3 (*Continued*)

Drug-Related Problem	Description	Example	Intervention
Drug interactions	Patient has a medical problem resulting from a drug-drug, drug-food or drug-laboratory interaction	Mild hyperkalemia after spironolactone added for HFrEF with concomitant ACE inhibitor use	Low potassium diet counseling with frequent follow-up to assess need for potassium binder patiromer
Drug use without indication	Patient is taking a drug for no medically valid indication	Ranitidine prescribed for stress ulcer prophylaxis during hospitalization for TAVR and continuously refilled post discharge in a patient with no documented GI indication	Comprehensive medication review to deprescribe and reduce inappropriate polypharmacy

AMI, acute myocardial infarction; CKD, chronic kidney disease; GI, gastrointestinal; HFrEF, heart failure with reduced ejection fraction; PCI, percutaneous coronary intervention; TAVR, transcatheter aortic valve replacement; VTE, venous thromboembolism.

concomitant hypertension. Results are summarized in Table 3.[45-48] Similarly, pharmacist participation in the treatment of acute myocardial infarction was shown to be independently associated with a 13.1-minute reduction in door and/or diagnosis to cardiac catheter lab time and an 11.5-minute reduction in door-to-balloon time.[49]

Cardiac arrests are another area for clinical pharmacists to enhance therapeutic outcomes and safety as errors in medication preparation, dosing, and prescribing can be common and lead to patient harm.[50] In a retrospective analysis of 74 arrest situations, pharmacist participation increased compliance with Advanced Cardiovascular Life Support guidelines (31.9% vs 59.3%; $P = 0.03$).[51] The most commonly detected areas of noncompliance were errors in dosing (30.4%), delay in intervention (26.1%), and deviation from treatment guideline (26.1%). A pilot study evaluating pharmacists as members of the Rapid Response Team showed delivery of 49 pharmacotherapy interventions, such as medication facilitation, dosing and/or therapy recommendations and addition or discontinuation of medications, during 32-individual situations.[52]

Chronic Care

Heart Failure

Projections show that the prevalence of heart failure will increase by 46% from 2012 to 2030[1] in part caused by longer exposure to risk factors such as hypertension, smoking, diabetes, obesity, and coronary artery disease and an aging population. Despite decades of evidence confirming the benefit of angiotensin converting enzyme inhibitors (ACE inhibitors), angiotensin II receptor blockers, aldosterone antagonists and select beta-blockers on morbidity and mortality among patients with left ventricular dysfunction, this guideline-directed medical therapy is underutilized in practice. Multiple studies have demonstrated that pharmacist interventions lead to higher rates of guideline-directed medical therapy prescribing and dose titration along with patient adherence to these prescribed therapies.[53-55] Since heart failure is to a large extent a medically managed disease clinical pharmacist into the care of heart failure patients can specifically decrease all-cause mortality and heart failure events.[56]

Other clinical pharmacist roles in heart failure are medication reconciliation, patient education, therapeutic drug monitoring, and prevention of medication errors or adverse drug events.[57] Integrating a pharmacist in the discharge process of heart failure patients results in a reduction of discrepancies and prescription errors.[58] Similarly, pharmacist participation

on inpatient heart failure teams has shown reduce the use of drugs that can worsen or exacerbate heart failure such as NSAIDs, calcium channel blockers and thiazolidinediones.[59]

Anticoagulation Management

As a drug class, anticoagulants are highly associated with preventable adverse drug events.[60]

Clinical pharmacist management of anticoagulation for the prevention and treatment of thromboembolic events, traditionally with warfarin, is well established.[61-63] Moreover, pharmacist-driven, physician-supported anticoagulation clinics improve anticoagulation control, and diminish rates of bleeding and thromboembolic events.[64,65] Health care costs, driven by decreased emergency department utilization and hospitalizations, are also reduced in pharmacist-driven anticoagulation clinics.[66]

Compared to warfarin direct oral anticoagulants (DOACs), such as rivaroxaban, apixaban, edoxaban, and dabigatran, offer predictable pharmacokinetics, fixed-dose regimens, fewer drug-drug interactions, and lack routine monitoring requirements. However, appropriate utilization of DOACs requires careful consideration of patient-specific factors such as age, renal function, weight, history gastrointestinal, or intracranial bleeding and adherence. Additionally, approved indications by the Food and Drug Administration are not as encompassing as warfarin and vary by agent. Driven by renal function and indication, inappropriate DOAC prescriptions are observed in up to 32.4% of patients.[67,68] In a retrospective analysis, Ashjian et al. found that patients in a pharmacist-led DOAC service were significantly more likely to receive a baseline prescription for an appropriately indicated DOAC and at an appropriate dose compared with the usual care group (93% vs 79.1%, $P = 0.009$).[69] This finding persisted at 3-6 month follow-up and improved adherence was also seen in the pharmacist cohort. As anticoagulation clinics shift from warfarin-based therapeutic drug monitoring, clinical pharmacists should be engaged in the decision-making process to determine a patient-tailored anticoagulant regimen at an appropriate dose, evaluate risk of bleeding complications and monitor adherence.

Practice Integration

Historically, a patient is referred to an outpatient clinical pharmacist to achieve tighter control for a single disease state. However cardiovascular risk reduction models that encompass dyslipidemia, hypertension, diabetes, weight loss, and tobacco cessation are certainly feasible via shared

medical appointments or pharmacist-coordinated care.[70,71] Inpatient clinical pharmacists can be dedicated to a role, such as coronary care or transitional care, or part of a subspecialty team, and not surprisingly hospitals utilizing cardiovascular credentialed pharmacists perform better on heart failure and acute myocardial infarction process of care measures.[72]

Some of the impediments to an expanded clinical pharmacist role include perceived lack of training by physicians, inadequate reimbursement and limited data on long term outcomes. However, the doctor of pharmacy degree has been the entry-level degree since the late 1990s and pharmacy school curriculum incorporates comprehensive medication management and patient-centered collaborative care.[73] As previously described, clinical pharmacists undergo additional post graduate training and rigorous continuing education to maintain credentials and board certification. Reimbursement models vary and are restricted as pharmacists are not nationally recognized as providers under Medicare Part B. Health care reform that promotes care delivery by pharmacists is vital.

Results from the first large randomized trial of pharmacist-driven CVD risk reduction (RxEACH) are promising and possibly indicative of future long term outcomes studies. Greater improvement in LDL-C, systolic blood pressure, hemoglobin A1c and smoking cessation at 3 months translated into a 21% difference in 10-year risk for CVD compared to usual care.[74]

Additional data from multicenter, randomized, prospective clinical pharmacist-driven studies on cardiovascular risk services to improve guideline adherence and telemedicine interventions to achieve CVD risk reduction are forthcoming.[75-77]

Conclusion

Table 3 describes 8 common cardiovascular drug-related problems accompanied by pharmacist solutions.[78] Pharmacists that have received appropriate training and credentialing are well suited to identify medication related problems and tailor pharmacotherapy to optimize outcomes. To prevent cardiovascular disease in high risk patients and decrease mortality among patients with established disease clinical pharmacists should be progressively utilized as care providers.

REFERENCES

1. Benjamin EJ, Virani SS, Callaway CW, et al. Heart disease and stroke statistics—2018 update: a report from the American Heart Association. Circulation 2018;137:e67–e492.

2. Brindis R, Rodgers GP, Handberg EM. President's page: team-based care: a solution for our health care delivery challenges. *J Am Coll Cardiol* 2011;57(9):1123–5. https://doi.org/10.1016/j.jacc.2011.02.003.
3. Dunn SP, Birtcher KK, Beavers CJ, et al. The role of the clinical pharmacist in the care of patients with cardiovascular disease. J Am Coll Cardiol 2015;66:2129–39.
4. The definition of clinical pharmacy. Pharmacotherapy 2008;28:816–7.
5. Chisholm-Burns MA, Lee JK, Spivey CA, et al. US pharmacists' effect as team members on patient care: systematic review and meta-analyses. Med Care 2010;48:923–33.
6. CfD Control. Prevention. Atlanta, GA: Centers for Disease Control and Prevention; 2017 National diabetes statistics report, 2017.
7. Mokdad AH, Ford ES, Bowman BA, et al. Prevalence of obesity, diabetes, and obesity-related health risk factors, 2001. JAMA 2003;289:76–9.
8. Casagrande SS, Fradkin JE, Saydah SH, Rust KF, Cowie CC. The prevalence of meeting A1C, blood pressure, and LDL goals among people with diabetes, 1988−2010. *Diabetes Care.* Aug 2013;36(8):2271–9.
9. Machado M, Bajcar J, Guzzo GC, Einarson TR. Sensitivity of patient outcomes to pharmacist interventions. Part I: systematic review and meta-analysis in diabetes management. Ann Pharmacother 2007;41:1569–82.
10. Hayward RA, Krein SL, Vijan S. Proactive case management of high-risk patients with type 2 diabetes mellitus by a clinical pharmacist: a randomized controlled trial. Am J Manag Care 2005;11:253.
11. Coast-Senior EA, Kroner BA, Kelley CL, Trilli LE. Management of patients with type 2 diabetes by pharmacists in primary care clinics. Ann Pharmacother 1998;32:636–41.
12. Rothman RL, Malone R, Bryant B, et al. A randomized trial of a primary care-based disease management program to improve cardiovascular risk factors and glycated hemoglobin levels in patients with diabetes. Am J Med 2005;118:276–84.
13. Fazel MT, Bagalagel A, Lee JK, Martin JR, Slack MK. Impact of diabetes care by pharmacists as part of health care team in ambulatory settings: a systematic review and meta-analysis. Ann Pharmacother 2017;51:890–907.
14. Hirsch JD, Bounthavong M, Arjmand A, et al. Estimated cost-effectiveness, cost benefit, and risk reduction associated with an endocrinologist-pharmacist diabetes intense medical management "tune-up" clinic. J Manag Care Spec Pharm 2017;23:318–26.
15. Jamal A, Phillips E, Gentzke AS, et al. Current Cigarette Smoking Among Adults—United States, 2016. Morb Mortal Wkly Rep 2018;67:53.
16. Burns DM. Epidemiology of smoking-induced cardiovascular disease. Prog Cardiovasc Dis 2003;46:11–29.
17. Babb S. Quitting smoking among adults—United States, 2000−2015. MMWR Morb Mortal Wkly Rep 2017;65(52):1457–64.
18. Augustine JM, Taylor AM, Pelger M, Schiefer D, Warholak TL. Smoking quit rates among patients receiving pharmacist-provided pharmacotherapy and telephonic smoking cessation counseling. J Am Pharm Assoc 2016;56:129–36.

19. Di Palo KE, Kish T. The role of the pharmacist in hypertension management. *Curr Opin Cardiol* 2018;33:382–7.
20. Tsuyuki RT, Houle SK, Charrois TL, et al. A randomized trial of the effect of pharmacist prescribing on improving blood pressure in the community: the Alberta clinical trial in optimizing hypertension (RxACTION). Circulation 2015. CIRCULATIONAHA.115.015464.
21. Hirsch JD, Steers N, Adler DS, et al. Primary care–based, pharmacist–physician collaborative medication-therapy management of hypertension: a randomized, pragmatic trial. Clin Ther 2014;36:1244–54.
22. Smith SM, Carris NW, Dietrich E, et al. Physician-pharmacist collaboration versus usual care for treatment-resistant hypertension. J Am Soc Hypertens 2016;10:307–17.
23. Lau R, Stewart K, McNamara KP, et al. Evaluation of a community pharmacy-based intervention for improving patient adherence to antihypertensives: a randomised controlled trial. BMC Health Serv Res 2010;10:34.
24. Chen Z, Ernst ME, Ardery G, Xu Y, Carter BL. Physician-pharmacist co-management and 24-hour blood pressure control. J Clin Hypertens 2013;15:337–43.
25. Hales CM, Carroll MD, Fryar CD, Ogden CL. Prevalence of *Obesity Among Adults and Yo*uth: United States, 2015-2016. US Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Health Statistics; 2017.
26. Ades PA, Savage PD. Obesity in coronary heart disease: An unaddressed behavioral risk factor. Prev Med 2017;104:117–9.
27. Lin JS, O'Connor E, Evans CV, Senger CA, Rowland MG, Groom HC. Behavioral counseling to promote a healthy lifestyle in persons with cardiovascular risk factors: a systematic review for the u.s. preventive services task force. Ann Intern Med 2014;161:568–78.
28. Reid F, Murray P, Storrie M. Implementation of a pharmacist-led clinic for hypertensive patients in primary care–a pilot study. Pharm World Sci 2005;27:202–7.
29. Thomas CE, Mauer EA, Shukla AP, Rathi S, Aronne LJ. Low adoption of weight loss medications: a comparison of prescribing patterns of antiobesity pharmacotherapies and SGLT2s. *Obesity* 2016;24:1955–61.
30. Wharton S, Serodio KJ. Next generation of weight management medications: implications for diabetes and CVD risk. Curr Cardiol Rep 2015;17:35.
31. Bohula EA, Scirica BM, Fanola C, et al. Design and rationale for the cardiovascular and metabolic effects of lorcaserin in overweight and obese patients-thrombolysis in myocardial infarction 61 (CAMELLIA-TIMI 61) trial. Am Heart J 2018;202:39–48.
32. Semla TP, Ruser C, Good CB, et al. Pharmacotherapy for Weight Management in the VHA. J Gen Intern Med 2017;32:70–3.
33. Grundy SM, Cleeman JI, Merz CNB, et al. Implications of recent clinical trials for the national cholesterol education program adult treatment panel III guidelines. Circulation 2004;110:227–39.
34. Ellis SL, Carter BL, Malone DC, et al. Clinical and economic impact of ambulatory care clinical pharmacists in management of dyslipidemia in older adults: the IMPROVE study. Pharmacotherapy 2000;20:1508–16.

35. Faulkner MA, Wadibia EC, Lucas BD, Hilleman DE. Impact of pharmacy counseling on compliance and effectiveness of combination lipid−lowering therapy in patients undergoing coronary artery revascularization: a randomized, controlled trial. Pharmacotherapy 2000;20:410–6.
36. Mazzolini TA, Icons BK, Schell EC, Seifert CF. Lipid levels and use of lipid-lowering drugs for patients in pharmacist-managed lipid clinics versus usual care in 2 VA Medical Centers. J Manag Care Pharm 2005;11:763–71.
37. Tsuyuki RT, Rosenthal M, Pearson GJ. A randomized trial of a community-based approach to dyslipidemia management: pharmacist prescribing to achieve cholesterol targets (RxACT study). Can Pharm J/Rev Pharm Can 2016;149:283–92.
38. Pokharel Y, Tang F, Jones PG, et al. Adoption of the 2013 American College of Cardiology/American Heart Association cholesterol management guideline in cardiology practices nationwide. JAMA Cardiol 2017;2:361–9.
39. Lin I, Sung J, Sanchez RJ, et al. Patterns of statin use in a real-world population of patients at high cardiovascular risk. J Manag Care Spec Pharm 2016;22:685–98.
40. Sabatine MS, Giugliano RP, Keech AC, et al. Evolocumab and clinical outcomes in patients with cardiovascular disease. N Engl J Med 2017;376:1713–22.
41. Schwartz G, Szarek M, Bhatt D, Bittner V, Diaz R, Edelberg J. The ODYSSEY OUTCOMES Trial: topline results alirocumab in patients after acute coronary syndrome. In: American College of Cardiology−67th Scientific Sessions; 2018.
42. Atanda A, Shapiro NL, Stubbings J, Groo V. Implementation of a new clinic-based, pharmacist-managed PCSK9 inhibitor consultation service. J Manag Care Spec Pharm 2017;23:918–25.
43. LaPointe NMA, Jollis JG. Medication errors in hospitalized cardiovascular patients. Arch Intern Med 2003;163:1461–6.
44. Schnipper JL, Kirwin JL, Cotugno MC, et al. Role of pharmacist counseling in preventing adverse drug events after hospitalization. Arch Intern Med 2006;166:565–71.
45. Montgomery K, Hall AB, Keriazes G. Impact of an emergency medicine pharmacist on time to thrombolysis in acute ischemic stroke. Am J Emerg Med 2016;34:1997–9.
46. Gosser RA, Arndt RF, Schaafsma K, Dang CH. Pharmacist impact on ischemic stroke care in the emergency department. J Emerg Med 2016;50:187–93.
47. Rech MA, Bennett S, Donahey E. Pharmacist participation in acute ischemic stroke decreases door-to-needle time to recombinant tissue plasminogen activator. Ann Pharmacother 2017;51:1084–9.
48. Jacoby JS, Draper HM, Dumkow LE, Farooq MU, DeYoung GR, Brandt KL. Emergency medicine pharmacist impact on door-to-needle time in patients with acute ischemic stroke. Neurohospitalist 2018;8:60–5.
49. Acquisto NM, Hays DP, Fairbanks RJT, et al. The outcomes of emergency pharmacist participation during acute myocardial infarction. J Emerg Med 2012;42:371–8.
50. Flannery AH, Parli SE. Medication errors in cardiopulmonary arrest and code-related situations. Am J Crit Care 2016;25:12–20.
51. Draper HM, Eppert JA. Association of pharmacist presence on compliance with advanced cardiac life support guidelines during in-hospital cardiac arrest. Ann Pharmacother 2008;42:469–74.

52. Groth CM, Acquisto NM. Pharmacists as members of the rapid response team. J Pharm Pract 2016;29:116–20.
53. Davis EM, Packard KA, Jackevicius CA. The pharmacist role in predicting and improving medication adherence in heart failure patients. J Manag Care Pharm 2014;20:741–55.
54. Bhat S, Kansal M, Kondos GT, Groo V. Outcomes of a Pharmacist-Managed Heart Failure Medication Titration Assistance Clinic. *Ann Pharmacother* Aug 2018;52 (8):724–32.
55. Jain A, Mills P, Nunn LM, et al. Success of a multidisciplinary heart failure clinic for initiation and up−titration of key therapeutic agents. Eur J Heart Fail 2005;7:405–10.
56. Gattis WA, Hasselblad V, Whellan DJ, O'connor CM. Reduction in heart failure events by the addition of a clinical pharmacist to the heart failure management team: results of the Pharmacist in Heart Failure Assessment Recommendation and Monitoring (PHARM) Study. Arch Intern Med 1999;159:1939–45.
57. Milfred−LaForest SK, Chow SL, DiDomenico RJ, et al. Clinical pharmacy services in heart failure: an opinion paper from the Heart Failure Society of America and American College of Clinical Pharmacy Cardiology Practice and Research Network. Pharmacotherapy 2013;33:529–48.
58. Eggink RN, Lenderink AW, Widdershoven JW, van den Bemt PM. The effect of a clinical pharmacist discharge service on medication discrepancies in patients with heart failure. Pharm World Sci 2010;32:759–66.
59. Suzuki M, Matsue Y, Izumi S, et al. Pharmacist-led intervention in the multidisciplinary team approach optimizes heart failure medication. Heart Vessels Jun 2018;33 (6):615–22.
60. Gurwitz JH, Field TS, Harrold LR, et al. Incidence and preventability of adverse drug events among older persons in the ambulatory setting. JAMA 2003;289:1107–16.
61. Gray DR, Garabedian-Ruffalo SM, Chretien SD. Cost-justification of a clinical pharmacist-managed anticoagulation clinic. SAGE Publications; 1985.
62. Wilt VM, Gums JG, Ahmed OI, Moore LM. Outcome analysis of a pharmacist−managed anticoagulation service. Pharmacotherapy 1995;15:732–9.
63. Conte R, Kehoe W, Nielson N, Lodhia H. Nine-year experience with a pharmacist-managed anticoagulation clinic. Am J Health Syst Pharm 1986;43:2460–4.
64. Bungard TJ, Gardner L, Archer SL, et al. Evaluation of a pharmacist-managed anticoagulation clinic: improving patient care. Open Med 2009;3:e16–21.
65. Chiquette E, Amato MG, Bussey HI. Comparison of an anticoagulation clinic with usual medical care: anticoagulation control, patient outcomes, and health care costs. Arch Intern Med 1998;158:1641–7.
66. Deanne H, Julianne B, Bethany H, et al. Health care expenditures and therapeutic outcomes of a pharmacist−managed anticoagulation service versus usual medical care. Pharmacotherapy 2011;31:686–94.
67. Miele C, Taylor M, Shah A. Assessment of direct oral anticoagulant prescribing and monitoring pre- and post-implementation of a pharmacy protocol at a community teaching hospital. Hosp Pharm 2017;52:207–13.

68. Ruiz Ortiz M, Muniz J, Raña Míguez P, et al. Inappropriate doses of direct oral anticoagulants in real-world clinical practice: prevalence and associated factors. A subanalysis of the FANTASIIA Registry. *EP Europace* 2017.
69. Ashjian E, Kurtz B, Renner E, Yeshe R, Barnes GD. Evaluation of a pharmacist-led outpatient direct oral anticoagulant service. Am J Health Syst Pharm 2017;74:483–9.
70. Cohen LB, Taveira TH, Khatana SA, Dooley AG, Pirraglia PA, Wu WC. Pharmacist-led shared medical appointments for multiple cardiovascular risk reduction in patients with type 2 diabetes. Diabetes Educ 2011;37:801–12.
71. Taveira TH, Wu WC, Martin OJ, Schleinitz MD, Friedmann P, Sharma SC. Pharmacist-led cardiac risk reduction model. Prev Cardiol 2006;9:202–8.
72. Dorsch MP, Lose JM, DiDomenico RJ. The effect of cardiovascular credentialed pharmacists on process measures and outcomes in myocardial infarction and heart failure. Pharmacotherapy 2014;34:803–8.
73. Jungnickel PW, Kelley KW, Hammer DP, Haines ST, Marlowe KF. Addressing competencies for the future in the professional curriculum. *AJPE* Dec 17 2009;73(8):156.
74. Tsuyuki RT, Al Hamarneh YN, Jones CA, Hemmelgarn BR. The effectiveness of pharmacist interventions on cardiovascular risk: the multicenter randomized controlled RxEACH trial. *J Am Coll Cardiol* 2016;67:2846–54.
75. Carter BL, Coffey CS, Chrischilles EA, et al. A cluster−randomized trial of a centralized clinical pharmacy cardiovascular risk service to improve guideline adherence. Pharmacotherapy 2015;35:653–62.
76. Carter BL, Levy BT, Gryzlak B, et al. A centralized cardiovascular risk service to improve guideline adherence in private primary care offices. Contemp Clin Trials 2015;43:25–32.
77. Zullig LL, Melnyk SD, Stechuchak KM, et al. The Cardiovascular Intervention Improvement Telemedicine Study (CITIES): rationale for a tailored behavioral and educational pharmacist-administered intervention for achieving cardiovascular disease risk reduction. Telemed e-Health 2014;20:135–43.
78. Strand LM, Morley PC, Cipolle RJ, Ramsey R, Lamsam GD. Drug-related problems: their structure and function. DICP 1990;24:1093–7.
79. Gale SE, Poon JL, Watson K. Antihyperglycemic Medications and Impact on Cardiovascular Outcomes: A Review of Current Evidence. *Pharmacotherapy* May 25 2018.

The role of pharmacists as interdisciplinary team members and direct patient care providers in both inpatient and outpatient settings is associated to a reduction cardiovascular risk and heart disease management.

Several perspectives can be drawn from this interesting manuscript.

First, inpatient clinical pharmacists can be dedicated to a role, such as coronary care or transitional care, or part of a subspecialty team. It has been shown, that hospitals utilizing cardiovascular credentialed pharmacists perform better on heart failure and acute myocardial infarction process of care measures.

Second, pharmacists that have received appropriate training and credentialing are well suited to identify medication related problems and tailor pharmacotherapy to optimize outcomes.

Third, there are some impediments to an expanded clinical pharmacist role, such as, perceived lack of training by physicians, inadequate reimbursement and limited data on long term outcomes. However, clinical pharmacists undergo additional post graduate training and rigorous continuing education to maintain credentials and board certification. Regarding reimbursement models vary and are restricted as pharmacists are not nationally recognized as providers under Medicare Part B. Health care reform that promotes care delivery by pharmacists is vital.

Results from the first large randomized trial of pharmacist-driven CVD risk reduction (RxEACH) are promising and possibly indicative of future long term outcomes studies. Greater improvement in LDL-C, systolic blood pressure, hemoglobin A1c and smoking cessation at 3 months translated into a 21% difference in 10-year risk for CVD compared to usual care.

Finally, the authors conclude that to prevent cardiovascular disease in high risk patients and decrease mortality among patients with established disease clinical pharmacists should be progressively utilized as care providers.

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