Diabetes and Cardiovascular Disease Interventions by Community Pharmacists: A Systematic Review

Charity D Evans, Erin Watson, Dean T Eurich, Jeff G Taylor, Erin M Yakiwchuk, Yvonne M Shevchuk, Alfred Remillard, and David Blackburn

Community pharmacists have been involved in activities related to the prevention and management of cardiovascular disease (CVD) and diabetes for many years, with research dating back to the late 1970s. Over the past decade, the number of community pharmacy practice publications has increased substantially. This increase is likely driven by several factors: recommendations that pharmacists should play a more active role in disease management,1-4 a push from within the profession to broaden the role of community pharmacists beyond the traditional dispensing and distribution functions,5 and an increasing need to generate objective evidence supporting these expanded roles.

There have been numerous studies reporting clinically significant benefits of community pharmacist interventions in diabetes and CVD. Some would argue, however, that major advancements in real-world practice have not followed suit.6 It has been suggested that this may be due to a lack of knowledge synthesis (eg, systematic reviews) or ineffective dissemination of the results.6 It is also possible that the published pharmacy research used as evidence for practice change has lacked the quality and/or generalizability necessary to successfully guide and support this change.

Although previous reviews have looked at community pharmacist inter-

Author information provided at end of text.

OBJECTIVE: To systematically review and assess the quality of studies evaluating community pharmacist interventions for preventing or managing diabetes or cardiovascular disease (CVD) and/or their major risk factors.

DATA SOURCES: A comprehensive literature search was performed using MEDLINE (1950-February 2011), EMBASE (1980-February 2011), International Pharmaceutical Abstracts (1970-February 2011), Cumulative Index to Nursing and Allied Health Literature (1982-June 2007), and Cochrane Central Register of Controlled Trials (1898-February 2011). Search terms included: community pharmacy(ies), community pharmacist(a), cardiovascular, diabetes, and intervention. The grey literature was searched using the ProQuest Dissertations and Theses, Theses Canada, and OAlster databases.

STUDY SELECTION AND DATA EXTRACTION: Articles published in English or French with all study designs were considered for the review. Studies were included if they contained interventions designed to reduce the incidence, risk, or mortality of CVD or diabetes; affect clinical indicators of CVD or diabetes mellitus (including hypertension, dyslipidemia, or hemoglobin A1c); and/or improve adherence to treatment strategies. Only studies involving interventions carried out primarily by pharmacists in community pharmacy settings were included. Study quality was assessed using a checklist validated for both randomized and nonrandomized studies.

DATA SYNTHESIS: A total of 4142 studies were initially identified, with 40 meeting our inclusion criteria. Eleven studies were randomized controlled trials, 4 were cluster randomized trials, and 2 studies had randomized before-after designs. The remaining studies were controlled before-after (n = 2), cohort (n = 4), and uncontrolled before-after (n = 17) designs. Interventions focused on diabetes (n = 12), hypertension (n = 9), medication adherence (n = 9), lipids (n = 5), evidence-based medication initiation or optimization (n = 3), risk factor prediction scores (n = 1), and body mass index (n = 1). All studies contained interventions focused at the patient level and the majority of studies (34/40) involved interventions directed at both the physician and patient. No specific intervention emerged as superior, and study quality was generally poor, making it difficult to determine the true effect of the interventions.

CONCLUSIONS: Poor study quality, time-intensive interventions, and unproven clinical significance warrant the need for further high-quality studies of community pharmacist interventions for preventing or managing diabetes or CVD and/or their major risk factors.

KEY WORDS: cardiovascular disease, community pharmacy, diabetes, intervention.


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ventions involving CVD or diabetes, they had a limited search strategy,5-11 were focused on a single risk factor,5,8,11,12 were not specific to community pharmacists (eg, hospital or clinic-based),5,8,11,13 or are now outdated.14 Thus, the purpose of this study was to systematically review the literature to summarize the breadth of community pharmacist interventions that have been developed to prevent or manage diabetes or CVD and/or their major risk factors, and to evaluate the quality of these studies.

Methods

SEARCH STRATEGY

A comprehensive literature search was performed by a librarian (EW) using MEDLINE (1950-February 2011), EMBASE (1980-February 2011), International Pharmaceutical Abstracts (1970-February 2011), and Cochrane Central Register of Controlled Trials (1898-February 2011). Search terms included community pharmacy(ies), community pharmacist(s), cardiovascular, diabetes, and intervention. A comprehensive list of search terms is available from the authors. Searches were initially carried out in June 2007 and then re-run to find additional, new articles in December 2007 and February 2011. In addition, the Cumulative Index to Nursing and Allied Health Literature was initially searched (1982-June 2007); however, partway through the project, the database provider changed, limiting search access and therefore it was not included after June 2007. The grey literature was searched using the ProQuest Dissertations and Theses, Theses Canada, and OAIster databases. Systematic review articles and bibliographies from original studies were hand searched for potentially relevant studies; experts and/or authors were not contacted. No publication date limits were used in the searches.

INCLUSION AND EXCLUSION CRITERIA

To maximize the inventory of pharmacy practice interventions that have been evaluated over the years, all studies published in English or French were considered for the review without regard for the study design. However, only full-text articles were included. Interventions must have been intended to reduce the incidence, risk, or mortality of CVD or diabetes; affect clinical indicators of CVD or diabetes mellitus (including hypertension, dyslipidemia, body weight, or hemoglobin A1c); and/or improve adherence to cardiovascular or diabetes therapies. Only studies involving interventions carried out by pharmacists in community pharmacy settings were included. Interventions that focused solely on patient screening and those that did not report measured outcomes were excluded.

RESULTS

Our search initially resulted in 4142 citations; 40 studies met the inclusion criteria (Figure 1). Interobserver agreement had a k value of 0.8753 for study inclusion among reviewers, indicating excellent agreement. Eleven studies were randomized controlled trials (RCTs) and 4 were cluster randomized (randomized by community pharmacy or district rather than individual subjects). Two studies18,40 that were labeled by the authors as an RCT have been categorized as a randomized before-after design, given the fact that no between-group comparisons were made. In each of the 4 cluster randomized studies identified, the authors inappropriately failed to account for the clustering effect in the analyses.24,25 The remaining studies were cohort (n = 4), controlled before-after (n = 2), and uncontrolled before-after (n = 17).

Studies were published between 1978 and 2010, with the majority published after 1999 (Table 1). Based on the primary endpoint, interventions focused on diabetes (n = 12),23-26 hypertension (n = 9),19,25,42 medication adherence (n = 9),43-51 and lipids (n = 5).18,52,53,57-59 The remaining stud-
ies focused on evidence-based medication initiation or optimization (n = 3),54-56 risk factor prediction scores (n = 1),54 risk factor prediction scores (n = 1),60 and body mass index (n = 1).61 Study lengths were variable and ranged from 2 to 57 months.

**INTerventions**

Based on the descriptions provided by the authors, interventions were classified as either patient-directed (pharmacist activities directed primarily toward patients) and/or physician-directed (pharmacist activities directed primarily toward physicians) (Table 2). All studies contained interventions involving patients, and the majority of studies (34/40) involved interventions directed at both the physician and patient. Overall, we found few differences between the types of interventions tested in the last decade compared to those in the 1970s50 and 1980s49 (Figure 2).

Patient-directed interventions were most commonly in the form of regular follow-up (38/40 [95.0%]) or education (38/40 [95.0%]), with only a small number (4/40 [10.0%]) using reminders (eg, to refill prescriptions). Education was provided by the pharmacist either verbally or through written materials and typically included information relating to the patient’s disease state and medications (eg, mechanism of action, adverse effects). Appropriate lifestyle management (diet, exercise, and smoking cessation) was frequently discussed, as was the importance of medication adherence. Follow-ups were conducted in person, by telephone, or mail, and generally occurred at predetermined intervals ranging from 2 weeks22,23,34,44,57 to 3 months.22 However, some interventions allowed for individualized impromptu follow-ups based on the need perceived by either the patient or pharmacist.27 Patient reminders included methods to remind patients to take or refill their medications, or “compliance packaging” of medications.48

The identification of drug-related problems and subsequent therapeutic recommendations was a key component of many physician-directed interventions (26/34 [76.5%]). Recommendations to physicians included therapy initiation, dosage adjustments, and the ordering of laboratory tests. Several interventions (15/40 [37.5%]) included notifying physicians of their patients’ involvement in, or progress with, the study through various means (eg fax, telephone). Finally, 9 of 40 (22.5%) interventions required the pharmacist to refer patients to their physicians for appropriate follow-up.

Interventions were typically time intensive, often requiring patient interviews, follow-up, and extensive collabora-
Table 1. Characteristics of Included Studies

<table>
<thead>
<tr>
<th>Study Reference</th>
<th>Study Design</th>
<th>Study Population</th>
<th>Intervention/Length</th>
<th>Primary Outcome</th>
<th>Intervention Categoryb (Sample Size)</th>
<th>Comparator</th>
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<th>Quality Score</th>
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<tbody>
<tr>
<td>Doucette (2009)R2</td>
<td>RCT</td>
<td>Type 2 diabetes</td>
<td>12 months</td>
<td>Change in mean A1C (%)</td>
<td>PT-ED; PT-FU; MD-JRP; MD-NOT (n = 36)</td>
<td>Usual care (n = 42)</td>
<td>Intervention: −0.27 (7.99 → 7.72) Comparator: +0.12 (7.91 → 8.03) (p = 0.27)</td>
<td>Low (17)</td>
</tr>
<tr>
<td>Krass (2007)R4</td>
<td>CRT</td>
<td>Type 2 diabetes</td>
<td>6 months</td>
<td>Change in mean A1C (%)</td>
<td>PT-ED; PT-FU; MD-JRP; MD-REF (n = 28 pharmacies)</td>
<td>Usual care (n = 28 pharmacies)</td>
<td>Intervention: −1.0 (8.9 → 7.9) Comparator: −0.3 (8.3 → 8.0) (p &lt; 0.01)</td>
<td>Low (17)</td>
</tr>
<tr>
<td>Fornos (2006)R5</td>
<td>RCT</td>
<td>Type 2 diabetes</td>
<td>13 months</td>
<td>Change in mean A1C (%)</td>
<td>PT-ED; PT-FU; MD-JRP (n = 58)</td>
<td>Usual care (n = 50)</td>
<td>Intervention: −0.5 (8.4 → 7.9) Comparator: +0.7 (7.8 → 8.5) (p &lt; 0.0001)</td>
<td>High (18)</td>
</tr>
<tr>
<td>Krass (2006)R6</td>
<td>Cohort</td>
<td>Type 2 diabetes</td>
<td>6 months</td>
<td>Change in mean A1C (%)</td>
<td>PT-ED; MD-JRP; MD-NOT (n = 39)</td>
<td>PT-ED; MD-DRP (n = 79)</td>
<td>ANCOVA showed a difference in A1C reduction of 0.27% between groups (p = 0.15)</td>
<td>Low (16)</td>
</tr>
<tr>
<td>Taylor (2005)R8</td>
<td>Controlled before-after</td>
<td>Type 2 diabetes</td>
<td>9 months</td>
<td>Change in mean A1C (%) from baseline</td>
<td>PT-1-EU; PT-1-U (n = 28)</td>
<td>Usual care (n = 111)</td>
<td>Intervention: −0.46 (7.86 → 7.40) Comparator: −0.03 (7.41 → 7.38) (p &lt; 0.05)</td>
<td>Low (14)</td>
</tr>
<tr>
<td>Robinson (2010)R2</td>
<td>Cohort</td>
<td>Hypertension</td>
<td>12 months</td>
<td>Change in mean BP from baseline</td>
<td>PT-ED; PT-FU; MD-NOT (n = 9 pharmacies; 180 pts.)</td>
<td>Usual care (n = 7 pharmacies; 196 pts.)</td>
<td>Systolic BP: Intervention: −9.9 mm Hg (151.5 → 141.6 mm Hg) Comparator: −2.6 mm Hg (151.5 → 148.7 mm Hg) (p &lt; 0.05) Diastolic BP: Intervention: −2.9 mm Hg (87.4 → 84.6 mm Hg) Comparator: −1.0 mm Hg (82.4 → 81.4 mm Hg) (p &lt; 0.16)</td>
<td>High (20)</td>
</tr>
<tr>
<td>Planas (2009)R5</td>
<td>RCT</td>
<td>Diabetes with hypertension</td>
<td>9 months</td>
<td>Change in mean systolic BP</td>
<td>PT-ED; PT-FU; MD-JRP; MD-NOT (n = 32)</td>
<td>Usual care (n = 20)</td>
<td>Intervention: −17.32 mm Hg (141.8 → 124.4 mm Hg) Comparator: +2.73 mm Hg (145.4 → 148.1 mm Hg) (p &lt; 0.003)</td>
<td>Low (17)</td>
</tr>
<tr>
<td>Zillich (2005)R8</td>
<td>CRT</td>
<td>Hypertension</td>
<td>3 months</td>
<td>Change in mean BP</td>
<td>PT-ED; PT-FU; MD-JRP (n = 6 pharmacies)</td>
<td>PT-FU (n = 6 pharmacies)</td>
<td>Systolic BP: Intervention: −13.4 mm Hg (151.5 → 138.1 mm Hg) Comparator: −9.0 mm Hg (151.6 → 142.6 mm Hg) (p &lt; 0.12) Diastolic BP: Intervention: −8.6 mm Hg (85.3 → 76.5 mm Hg) Comparator: −5.6 mm Hg (85.3 → 79.7 mm Hg) (p &lt; 0.03)</td>
<td>Low (16)</td>
</tr>
<tr>
<td>Study</td>
<td>Type</td>
<td>Intervention</td>
<td>Outcome Measures</td>
<td>Results</td>
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<tr>
<td>Garcia (2002)</td>
<td>RCT</td>
<td>Hypertension</td>
<td>Proportion of pts. with controlled BP</td>
<td>Baseline: 50%</td>
<td>Post-intervention: 60%</td>
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</tr>
<tr>
<td>Blankensopp (2000)</td>
<td>CRT</td>
<td>Hypertension</td>
<td>Proportion of pts. with controlled BP</td>
<td>Baseline: 45%</td>
<td>Post-intervention: 55%</td>
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<tr>
<td>Park (1996)</td>
<td>Randomized before-after</td>
<td>Hypertension</td>
<td>Mean systolic and diastolic BP</td>
<td>Baseline: 120/80</td>
<td>Post-intervention: 110/70</td>
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<tr>
<td>Paulos (2005)</td>
<td>Randomized before-after</td>
<td>Dyslipidemia</td>
<td>Change in mean TC from baseline</td>
<td>Baseline: 200</td>
<td>Post-intervention: 190</td>
<td></td>
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<tr>
<td>MEDMAN study (2007)</td>
<td>RCT</td>
<td>CHD</td>
<td>Proportion of pts. receiving appropriate secondary prevention management for CHD</td>
<td>Baseline: 50%</td>
<td>Post-intervention: 60%</td>
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</tbody>
</table>

**Notes:**
- A1C = hemoglobin A1C; ANCOVA = analysis of covariance; BMI = body mass index; BP = blood pressure; CAD = coronary artery disease; CHD = coronary heart disease; CRT = cluster randomized trial; CV = cardiovascular; LDL-C = low-density lipoprotein cholesterol; MEMS = medication event monitoring system; MPR = medication possession ratio; N/A = not applicable; NS = not significant; RCT = randomized controlled trial; SBBG = self blood glucose monitoring; TC = total cholesterol.
- *If no primary outcome specified, we used the first outcome reported in the Results section, or outcome used in power calculation (if performed).
- Intervention categories: MD-DRP = identification and reporting of drug-related problems and subsequent recommendations made to patient's physician; MD-NOT = notification to the physician about patient's participation or progress in the study; MD-REF = patients were referred to their physician by the pharmacist; PT-ED = patient-directed education; PT-FU = regular patient follow-up; PT-RE = medication reminders or compliance packaging.
- *Based on reported results and statistics. In some cases, statistical significance not reported.
- Out of 32 possible points; based on Downs and Black checklist (high ≥18/32 [56%]; low <18/32).
<table>
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</tr>
</thead>
<tbody>
<tr>
<td>Tsuyuki (2002)58</td>
<td>RCT</td>
<td>High risk for CV events</td>
<td>16 weeks</td>
<td>Composite: physician orders fasting lipid panel, initiates new cholesterol-lowering drug, or increases dose of current cholesterol drug</td>
<td>PT-ED; PT-FU; MD-DRP; MD-NOT (n = 344)</td>
<td>PT-ED; PT-FU (n = 331)</td>
<td>Intervention: 57% (196/344) Comparator: 31% (102/331) OR 3.0, 95% CI 2.2 to 4.1 (p &lt; 0.001)</td>
<td>High (25)</td>
</tr>
<tr>
<td>Nola (2000)62</td>
<td>Controlled before-after</td>
<td>Known CAD or lipid levels requiring treatment</td>
<td>6 months</td>
<td>Change in risk factor prediction scores from baseline</td>
<td>PT-ED; PT-FU; MD-DRP (n = 25)</td>
<td>Usual care (n = 26)</td>
<td>Intervention: -0.6 (17.0 → 16.4) Comparator: +0.6 (16.5 → 17.1) (p = NS)</td>
<td>Low (13)</td>
</tr>
<tr>
<td>Eussean (2010)81</td>
<td>RCT</td>
<td>New users of statins</td>
<td>12 months</td>
<td>Discontinuation rates 1 year</td>
<td>PT-ED; PT-FU (n = 513)</td>
<td>Usual care (n = 503)</td>
<td>Intervention: 23% Comparator: 26% HR 0.84 (95% CI 0.65 to 1.10)</td>
<td>High (25)</td>
</tr>
<tr>
<td>Nielert (2009)43</td>
<td>RCT</td>
<td>Pts. at least 7 days overdue for diabetes, hypertension, lipid, depression, or psychosis medication</td>
<td>7 months</td>
<td>Time to refill (days)</td>
<td>Phone group: PT-FU; PT-RE (n = 1018) Fax group: MD-NOT (pt. late for refill) (n = 1010)</td>
<td>Usual care (n = 1014)</td>
<td>Phone group: median 108 days Comparator: median 106 days Phone vs comparator: HR 0.93 (97.5% CI 0.62 to 1.06) Fax vs comparator: HR 0.67 (95.3% CI 0.76 to 1.00) Phone vs fax: HR 0.93 (95% CI 0.83 to 1.05)</td>
<td>High (20)</td>
</tr>
<tr>
<td>Vrijens (2008)44</td>
<td>CRT</td>
<td>Pts. taking atorvastatin for at least 3 months</td>
<td>12 months</td>
<td>Proportion of days that the pill bottle (MEMS) was opened</td>
<td>PT-ED; PT-FU; PT-RE (n = 194)</td>
<td>Usual care (n = 198)</td>
<td>Intervention: 95.89% Comparator: 89.37% HR 0.93 (95% CI 0.83 to 1.05) (p &lt; 0.001)</td>
<td>High (16)</td>
</tr>
<tr>
<td>Bouvy (2003)66</td>
<td>RCT</td>
<td>Heart failure, pts. taking a loop diuretic</td>
<td>6 months</td>
<td>Medication nonadherence (days without medication as identified by MEMS)</td>
<td>PT-ED; PT-FU; MD-NOT (n = 74)</td>
<td>Usual care (n = 78)</td>
<td>Intervention: 140/7656 days Comparator: 337/6196 days RR 0.32 (95% CI 0.19 to 0.55)</td>
<td>Low (15)</td>
</tr>
<tr>
<td>Skaer (1993)48</td>
<td>RCT</td>
<td>Type 2 diabetes, newly diagnosed; pts. receiving a first prescription for glyburide 5 mg bid</td>
<td>360 days</td>
<td>Adherence (MPR)</td>
<td>PT-RE, mail reminder (n = 79) Compliance packaging (n = 53) Reminder + packaging (n = 49)</td>
<td>Usual care (n = 78)</td>
<td>Mail 0.73; compliance packaging 0.71; mail + compliance 0.87; comparator 0.58 (p ≤ 0.05 for all groups vs comparator group)</td>
<td>Low (12)</td>
</tr>
</tbody>
</table>
Studies without a control group

<table>
<thead>
<tr>
<th>Author</th>
<th>Type</th>
<th>Duration</th>
<th>Primary Outcome</th>
<th>Comparator</th>
<th>Intervention</th>
<th>Comparator</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ascione (1965)</td>
<td>RCT</td>
<td>4 months</td>
<td>Proportion of pts. refilling prescriptions late</td>
<td>PT-ED; PT-FU; PT-RE (n = 52)</td>
<td>Usual care (n = 50)</td>
<td>Intervention: 41% filled prescriptions late Comparator: 53% filled prescriptions late (p = NS)</td>
</tr>
<tr>
<td>McKenney (1970)</td>
<td>Cohort</td>
<td>4 months</td>
<td>Proportion of adherent pts. (receiving ≥15% of prescribed dose)</td>
<td>PT-ED; PT-FU; MD-NOT (n = 70)</td>
<td>Usual care (n = 66)</td>
<td>Intervention: 62.9% (44/70) Comparator: 34.8% (23/69) (p &lt; 0.005)</td>
</tr>
<tr>
<td>Turnacilar (2009)</td>
<td>Uncontrolled before-after</td>
<td>3 months</td>
<td>Change in mean fasting blood glucose</td>
<td>PT-ED; PT-FU; MD-3RP (n = 43)</td>
<td>N/A</td>
<td>At study end: -38.5 mg/dL (167.2 mg/dL → 128.7 mg/dL) (p &lt; 0.001)</td>
</tr>
<tr>
<td>Fera (2008)</td>
<td>Uncontrolled before-after</td>
<td>Diabetes</td>
<td>Minimum 3 months</td>
<td>Change in mean A1C (%) from baseline</td>
<td>PT-ED; PT-FU; MD-NOT (n = 914)</td>
<td>N/A</td>
</tr>
<tr>
<td>Garrett (2009)</td>
<td>Uncontrolled before-after</td>
<td>Diabetes</td>
<td>Minimum 3 months</td>
<td>Change in mean A1C (%) from baseline</td>
<td>PT-ED; PT-FU; MD-3RP; MD-NOT; MD-REF (n = 256)</td>
<td>N/A</td>
</tr>
<tr>
<td>Cranor (2009)</td>
<td>Uncontrolled before-after</td>
<td>Diabetes</td>
<td>7-9 months</td>
<td>Change from baseline in proportion of patients with A1C ≤7.0%</td>
<td>PT-ED; PT-FU; MD-1EF (n = 85)</td>
<td>N/A</td>
</tr>
<tr>
<td>Cranor (2009)</td>
<td>Up to 5 years</td>
<td></td>
<td>Change from baseline in mean A1C (%)</td>
<td>PT-ED; PT-FU; MD-3RP; MD-NOT (n = 47)</td>
<td>N/A</td>
<td>After last follow-up: +18.1% (45.5% to 63.6%) (p = 0.32)</td>
</tr>
<tr>
<td>Nau (2002)</td>
<td>Uncontrolled before-after</td>
<td>Type 2 diabetes</td>
<td>9 months (median)</td>
<td>Change from baseline in mean A1C (%)</td>
<td>PT-ED; PT-FU; MD-3RP; MD-NOT (n = 47)</td>
<td>N/A</td>
</tr>
<tr>
<td>Berringer (1999)</td>
<td>Uncontrolled before-after</td>
<td>Diabetes</td>
<td>12 months</td>
<td>Change from baseline in proportion of pts. with at least once-daily SBGM</td>
<td>PT-ED; PT-FU; MD-3RP (n = 62)</td>
<td>N/A</td>
</tr>
<tr>
<td>Fincham (1998)</td>
<td>Uncontrolled before-after</td>
<td>Diabetes</td>
<td>2 months</td>
<td>Proportion of pts. having a foot examination performed vs baseline</td>
<td>PT-ED (n = 51)</td>
<td>N/A</td>
</tr>
</tbody>
</table>

A1C = hemoglobin A1c; ANCOVA = analysis of covariance; BMI = body mass index; BP = blood pressure; CAD = coronary artery disease; CHD = coronary heart disease; CRT = cluster randomized trial; CV = cardiovascular; LDL-C = low-density lipoprotein cholesterol; MEMS = medication event monitoring system; MPR = medication possession ratio; N/A = not applicable; NS = not significant; RCT = randomized controlled trial; SBGM = self blood glucose monitoring; TC = total cholesterol.

*If no primary outcome specified, we used the first outcome reported in the Results section, or outcome used in power calculation if performed.

*Intervention categories: MD-DRP = identification and reporting of drug-related problems and subsequent recommendations made to patient’s physician; MD-NOT = notification to the physician about patient’s participation or progress in the study; MD-REF = patients were referred to their physician by the pharmacist; PT-ED = patient-directed education; PT-FU = regular patient follow-up; PT-RE = medication reminders or compliance packaging.

*Based on reported results and statistics. In some cases, statistical significance not reported.

*Out of 32 possible points; based on Downs and Black checklist18 (high ≥18/32 [56%]; low <18/32).17

(continued on page 622)
<table>
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<tr>
<th>Reference</th>
<th>Study Design</th>
<th>Study Population</th>
<th>Intervention Length</th>
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</thead>
<tbody>
<tr>
<td>Lai (2007)36</td>
<td>Uncontrolled before-after</td>
<td>Hypertension</td>
<td>9 months</td>
<td>Change from baseline in mean BP</td>
<td>PT-ED; PT-FU; MD-JRP (n = 103)</td>
<td>N/A</td>
<td>After 9 months:</td>
<td>N/A</td>
</tr>
<tr>
<td>Oparah (2006)37</td>
<td>Uncontrolled before-after</td>
<td>Hypertension</td>
<td>6 months</td>
<td>Change from baseline in mean BP</td>
<td>PT-ED; PT-FU; MD-JRP (n = 42)</td>
<td>N/A</td>
<td>At study end:</td>
<td>N/A</td>
</tr>
<tr>
<td>Bluml (2000)57</td>
<td>Uncontrolled before-after</td>
<td>Dyslipidemia</td>
<td>24.6 months (mean)</td>
<td>Change from baseline in mean TC</td>
<td>PT-ED; PT-FU; MD-JRP; MD-NOT (n = 397)</td>
<td>N/A</td>
<td>At study end:</td>
<td>N/A</td>
</tr>
<tr>
<td>Shibley (1990)58</td>
<td>Uncontrolled before-after</td>
<td>Hyperlipidemia</td>
<td>12 months</td>
<td>Change from baseline in mean TC</td>
<td>PT-ED; PT-FU; MD-JRP; MD-NOT (n = 25)</td>
<td>N/A</td>
<td>At study end:</td>
<td>N/A</td>
</tr>
<tr>
<td>Ibrahim (2007)59</td>
<td>Uncontrolled before-after</td>
<td>Dyslipidemia, not previously diagnosed</td>
<td>6 months</td>
<td>Change from baseline in mean TC</td>
<td>PT-ED; PT-FU; MD-REF (n = 57)</td>
<td>N/A</td>
<td>At study end:</td>
<td>N/A</td>
</tr>
<tr>
<td>Semchuk (2007)60</td>
<td>Uncontrolled before-after</td>
<td>High risk for CV events</td>
<td>24 weeks</td>
<td>Proportion of pts. with a dose increase or addition of any CV risk-lowering drug compared to baseline</td>
<td>PT-ED; PT-FU; MD-JRP; MD-NOT; MD-REF (n = 217)</td>
<td>N/A</td>
<td>48.1% achieved primary endpoint (p value not reported)</td>
<td>N/A</td>
</tr>
<tr>
<td>Tsuyuki (2004)52 (SCRIP-plus)</td>
<td>Uncontrolled before-after</td>
<td>Very high risk for CV events</td>
<td>6 months</td>
<td>Change from baseline in mean LDL-C</td>
<td>PT-ED; PT-FU; MD-JRP (n = 419)</td>
<td>N/A</td>
<td>After 6 months:</td>
<td>N/A</td>
</tr>
<tr>
<td>Yamada (2005)53</td>
<td>Uncontrolled before-after</td>
<td>Not being treated for dyslipidemia or hypertension</td>
<td>1 year after study end</td>
<td>Change in LDL-C</td>
<td>PT-ED; PT-FU; MD-REF (n = 282 distributed over 2 cohorts)</td>
<td>N/A</td>
<td>Cohort 1: +0.1 kg/m² (29.6 → 29.7 kg/m²) (p = NS)</td>
<td>N/A</td>
</tr>
<tr>
<td>Krass (2003)61</td>
<td>Uncontrolled before-after</td>
<td>Not being treated for dyslipidemia or hypertension</td>
<td>3 months</td>
<td>Change from baseline in mean BMI</td>
<td>PT-ED; PT-FU; MD-REF (n = 282 distributed over 2 cohorts)</td>
<td>N/A</td>
<td>Cohort 2: -0.1 kg/m² (30.0 → 29.9 kg/m²) (p = NS)</td>
<td>N/A</td>
</tr>
</tbody>
</table>
A1C = hemoglobin A1C; ANCOVA = analysis of covariance; BMI = body mass index; BP = blood pressure; CAD = coronary artery disease; CHD = coronary heart disease; CRT = cluster randomized trial; CV = cardiovascular; LDL-C = low-density lipoprotein cholesterol; MEMS = medication event monitoring system; MPR = medication possession ratio; N/A = not applicable; NS = not significant; RCT = randomized controlled trial; SBGM = self blood glucose monitoring; TC = total cholesterol.

If no primary outcome specified, we used the first outcome reported in the Results section, or outcome used in power calculation (if performed).

*Intervention categories: MD-DRP = identification and reporting of drug-related problems and subsequent recommendations made to the patient’s physician; MD-NOT = notification to the physician about the patient’s participation or progress in the study; MD-REF = patients were referred to their physician by the pharmacist; PT-ED = patient-directed education; PT-FU = regular patient follow-up; PT-RE = medication reminders or compliance packaging.

*Based on reported results and statistics. In some cases, statistical significance not reported.

*Out of 32 possible points, based on Downs and Black checklist [16] (high ≥18/32 [56%]; low <18/32). [17]

A1

<table>
<thead>
<tr>
<th>Study</th>
<th>Type of Intervention</th>
<th>N/A</th>
<th>N/A</th>
<th>N/A</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ai (2003)</td>
<td>Uncontrolled ...</td>
<td>65</td>
<td>PT-ED; PT-FU; MD-NOT (n = 149)</td>
<td>At study end: +15.3% (40.7% → 56.0%) (p &lt; 0.05)</td>
</tr>
<tr>
<td>Taylor (2003)</td>
<td>Uncontrolled ...</td>
<td>36</td>
<td>PT-ED; PT-FU; MD-DRP (n = 8)</td>
<td>At study end: +75% (2/8 → 8/8) (p value not reported)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Study</th>
<th>Type of Intervention</th>
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*Based on reported results and statistics. In some cases, statistical significance not reported.

*Out of 32 possible points, based on Downs and Black checklist [16] (high ≥18/32 [56%]; low <18/32). [17]
96%. In this case, the improvement was statistically significant, but the patient population appeared to be adherent regardless of the intervention.

STUDY QUALITY

Quality scores for the studies evaluated (only those with a control group) were poor, as only 8 of 23 (34.8%) studies received a score of 18 out of 32 (56%) or greater. All 8 studies were published in the last decade. Sample sizes ranged from 8 to 1493. Only 14 of 40 (35.0%) studies described an a priori power calculation, and only 6 of these achieved adequate power for analysis of the primary endpoint.

Studies published from 2004 to 2009 scored relatively higher on items assessing reporting quality than did studies published before 2004. In most cases, poorly reported studies lacked an adequate description and/or comparison of subjects at baseline, and did not report p values (or confidence intervals) for the study results. Identification of predetermined outcomes was poor, particularly in the uncontrolled before-after studies, where only 9 of 17 (52.9%) of these studies clearly specified a primary endpoint.

Randomized studies scored relatively better than the nonrandomized designs, as expected, but only 7 of 17 achieved a score of 18 out of 32 or higher. Of the randomized design studies, only 1 reported binding of the personnel involved in data collection and analysis, and only 3 reported blinding of the intervention allocation. Intention-to-treat analysis was mentioned in 9 of 17 (52.9%) randomized studies; however, only 5 of these studies performed an appropriate intention-to-treat analysis.

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient-directed</td>
<td></td>
</tr>
<tr>
<td>education</td>
<td>Initial education and/or counseling session provided directly to pts.</td>
</tr>
<tr>
<td>follow-up</td>
<td>Regular contact with pts. (in-person, phone, mail)</td>
</tr>
<tr>
<td>reminders</td>
<td>Medication reminders and/or compliance packaging (no pt. education)</td>
</tr>
<tr>
<td>Physician-directed</td>
<td></td>
</tr>
<tr>
<td>drug-related problems—recommendations</td>
<td>Identification of actual or potential drug-related problems and/or therapeutic recommendations made to physician by the pharmacist in response to identified drug-related problems</td>
</tr>
<tr>
<td>notification</td>
<td>Physician notified about pt.'s study involvement and/or progress (no specific recommendations made)</td>
</tr>
<tr>
<td>referral</td>
<td>Pt. referred to physician by pharmacist</td>
</tr>
</tbody>
</table>

![Table 2. Categorization of Interventions](table2.png)

**Figure 2.** Proportion of interventions published by decade. Patient Education: initial education and/or counseling session provided directly to patient; Patient Follow-up: regular contact with patients (in-person, phone, mail); Patient Reminders: medication reminders and/or compliance packaging (no patient education provided); Drug-Related Problems/Recommendations: identification of actual or potential drug-related problems and/or therapeutic recommendations made to physician by the pharmacist in response to identified drug-related problems; Physician Notification: physician notified about patient’s study involvement and/or progress (no specific recommendations made); Physician Referral: patient referred to physician by pharmacist.
Discussion

To the best of our knowledge, this is the first systematic review that has summarized interventions specific to community pharmacists that focus on both diabetes and CVD and all their major risk factors. All identified studies involved patient-directed interventions such as education and follow-up. Most studies also involved physician-directed interventions, the most common of which was the identification of drug-related problems and provision of therapeutic recommendations. The majority of studies were published in the last 10 years, although the interventions have remained similar over the past 30 years. Studies were generally of poor quality and evaluated interventions that typically appeared to be time-intensive.

Poor study quality has plagued pharmacy practice research studies for years,

and problems range from poor design to poor reporting. Although RCTs are considered the gold standard for the evaluation of treatment efficacy and effectiveness, the majority of studies in this review used a nonrandomized design. In fact, 17 of the studies did not use a control group, and 2 studies with a control group made no between-group comparisons. Although it may be challenging to find adequate controls for studies conducted in small community pharmacy settings, the lack of a control group makes it difficult to conclude a causal relationship between the intervention being evaluated and the subsequent outcome(s).

Based on the studies examined in this review, reporting of results seems to have improved over time, and is likely due to the development of guidelines for the reporting of both randomized and observational studies. However, poor reporting was still an issue even in more recent publications, especially in the nonrandomized studies. The lack of a clearly identified primary outcome and appropriate statistical comparisons (i.e., p values and confidence intervals) was common and made it difficult to evaluate and interpret the results. In some cases the authors suggested favorable outcomes that were either inconsistent with the results reported, or not supported by statistical evidence.

A major challenge when designing pharmacy research is the matter of blinding. In most cases, it is difficult for either the subjects or researchers to be blinded, especially if the intervention involves direct patient care. However, because blinding is a factor in most quality assessment scores, some argue that the quality of pharmacy practice studies will always be underestimated. Blinding those responsible for the data collection and analysis, and the concealment of intervention allocation in RCTs, can reduce bias and improve study quality; however, these strategies were rarely undertaken in published studies.

Study quality was likely influenced by several factors. First, contemporary techniques to minimize bias and confounding may have been unknown to many investigators who conducted their research before the 1990s. Indeed, we found that studies published since 2000 were generally of higher quality compared to all others. Interestingly, we could not identify major differences in the types of interventions used in lower-quality versus high-quality studies. Similarly, we could not find any notable differences in the types of pharmacist interventions tested throughout the years. For example, in 1978, McKenney et al.

evaluated a pharmacist intervention that was completely comparable to more recent interventions published in the pharmaceutical care era.

The majority of interventions involved in-depth consultations with individual patients (and subsequently physicians or other health-care professionals) for the purpose of identifying and resolving actual and potential drug-related problems. In general, these strategies appeared to be time-intensive, and their impact on patient outcomes remains unproven. Also, the extent to which these strategies could be integrated into current community pharmacy settings is not clear. Only 3 studies commented on the impact the intervention had on staffing and time of employees. Even highly successful interventions will have little benefit if they cannot be implemented in real-world settings.

We believe that more research is needed to evaluate strategies that can be implemented in current community pharmacy practice.

A limitation of our search strategy is that we included only full-text articles published in English or French. Although 6 studies were excluded based on language, it is unlikely that the intervention(s) being evaluated in those studies differed significantly from those in the included studies. Categorization of interventions and quality assessments were based on what was reported in the published studies, and we did not contact authors for extra details. As with any systematic review, there is the potential for publication bias.

The quality checklist used has its own limitations. The lack of reference standard for the total quality score forces reviewers to make a judgment call on what they consider to be an acceptable level of quality. We chose a score of 18/32 or higher based on a previously published review, although much lower acceptable levels of quality have also been used. The checklist also required subjective judgments, which were often made more difficult by the poor reporting of some studies. However, by using 2 independent reviewers and a third to resolve any discrepancies, we can have confidence in our assessments.

Summary

The majority of community pharmacy studies reviewed from the past 30 years appear to show benefit in the reduction or management of diabetes or CVD and their risk factors. However, study quality was generally poor, interven-
tions were time intensive, and none of the studies demonstrated any benefits to major health outcomes. Therefore, the clinical importance of these interventions remains unclear, and further well-designed, well-conducted studies are needed to guide community pharmacists in this important area of practice.

**Conflict of interest:** Authors reported none

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We thank Darcy Lamb MSc for his help in reviewing abstracts and studies.

**References**

Diabetes and Cardiovascular Disease Interventions by Community Pharmacists


Intervenciones en el Tratamiento de Diabetes y Enfermedad Cardiovascular por Farmacéuticos Comunitarios: Un Repaso Sistémático

CD Evans, E Watson, DT Eurich, JG Taylor, EM Yakivchuk, YM Shevchuk, A Remillard, y D Blackburn

**OBJETIVO:** Repasar sistemáticamente y evaluar la calidad de los estudios que reportaron intervenciones hechas por farmacéuticos en la prevención y el manejo de la diabetes y enfermedad cardiovascular y sus factores de riesgo mayores.

**FUENTES DE INFORMACIÓN:** Se condujo una búsqueda comprensiva usando MEDLINE, EMBASE, Abstracts Farmacéuticos Internacionales, Cumulative Index to Nursing and Allied Health Literature (CINAHL), y el Cochrane Central Register to Controlled Trials. También se realizó una búsqueda de la literatura "gris" usando los bancos de datos llamados ProQuest Dissertations and Thesis, Theses Canada, y OAlster.

**SELECCIÓN DE ESTUDIOS Y EXTRACCIÓN DE DATOS:** Artículos publicados en idiomas inglés o francés fueron considerados para reseña. Se incluyó estudios si estos contenían intervenciones diseñadas que redujeron la incidencia, el riesgo o la mortalidad de las enfermedades cardiovasculares o diabetes; indicadores clínicos que afectaron las enfermedades cardiovasculares o diabetes (incluyendo hipertensión, dislipidemia o ANA); y/o mejoraron las estrategias de adherencia al tratamiento. Se incluyó sólo aquellos estudios que contuvieron intervenciones que fueron llevadas a cabo principalmente por farmacéuticos en farmacias comunitarias. Se evaluó la calidad de estudios utilizando una lista de verificación para validar los estudios aleatorios y no aleatorios.

**SÍNTESIS DE DATOS:** Se identificaron inicialmente un total de 4142 estudios y 40 de estos cumplieron con los criterios de inclusión. Once de estos fueron estudios aleatorios controlados, cuatro fueron estudios aleatorios agrupados y dos fueron diseños aleatorios de antes-y-después. Los demás fueron estudios controlados de antes-y-después (n = 2), cohorte (n = 4) y no controlados de antes-y-después (n = 17). Las intervenciones enfocaron en diabetes (n = 12), hipertensión (n = 7), adherencia a medica-

**RESUMEN:**

**OBJETIVO:** Revisar la literatura y la calidad de los estudios evaluando las intervenciones de los farmacéuticos practicando en el cuidado comunitario de un nivel de la prevención o del tratamiento de la diabetes, las malas condiciones cardiovasculares y las enfermedades de diabetes.

**FUENTES DE INFORMACIÓN:** Una búsqueda documental efectuada en las bases de datos MEDLINE, EMBASE, International Pharmaceutical Abstracts, CINAHL, y en el registro central Cochrane para las revisiones clínicas. Las bases de datos OAlster, Theses Canada y ProQuest (dissertaciones y tesis) también han sido consultadas para identificar la literatura gris.

**SELECCIÓN DE INFORMACIÓN:** Todos los artículos publicados en inglés o francés en la literatura revisada para esta revisión. Los estudios incluyeron aquellos que describieron intervenciones que fueron llevadas a cabo principalmente por farmacéuticos en farmacias comunitarias.

**SÍNTESIS DE DATOS:** Se seleccionaron inicialmente un total de 4142 estudios y 40 de estos cumplieron con los criterios de inclusión. Once de estos fueron estudios aleatorios controlados, cuatro fueron estudios aleatorios agrupados y dos fueron diseños aleatorios de antes-y-después. Los demás fueron estudios controlados de antes-y-después (n = 2), cohorte (n = 4) y no controlados de antes-y-después (n = 17). Las intervenciones enfocaron en diabetes (n = 12), hipertensión (n = 7), adherencia a medicamentos (n = 9), lidopérgos (n = 5), iniciación u optimización de medicamentos basado en evidencia (n = 3), pronóstico de predicción de factores de riesgo (n = 1) e índice de masa corporal (n = 1). Todos los estudios contenían intervenciones que fueron aplicadas al nivel del paciente y la mayoría (34/40) fueron dirigidas a los médicos y pacientes. No hubo intervenciones específicas que hubieran sido superiorables y la calidad de los estudios fue generalmente de pobre calidad, haciendo difícil determinar el efecto verdadero de las intervenciones.

**CONCLUSIONES:** Estudios de calidad pobre, intervenciones de tiempo intensivos e importancia clínica no probada justifican la necesidad de realizar más estudios de alta calidad.