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Interventions in Chronic Disease Management: a Review of the Literature on the Role of Community Pharmacists.

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ABSTRACT

There is a limited number of studies evaluate the performance of existing chronic diseases management and its outcomes in community pharmacy. This study aimed to evaluate published evidence in chronic disease management in community pharmacy internationally. A literature review was performed covering the period from January 2000 to March 2013 using EMBASE, Medline and International Pharmaceutical Abstracts. Published studies involving interventions carried out by community pharmacists with the evaluation of interventions in clinical, humanistic or economic outcomes focusing on five chronic diseases, namely; diabetes, cardiovascular disease, asthma, mental illness and cancer were included. Duplicate articles were removed electronically (Endnote®) and the remaining articles were screened to assess their eligibility according to the inclusion and exclusion criteria. Full copies of the potential eligible articles were obtained and each study was further reviewed by the reviewers independently. From 2,973 articles identified, 91 manuscripts were included in the final analysis. Limited number of interventions in cancer and mental illness was identified. Approximately 87% of total studies reported interventions in population with existing diseases. Less than 10% reported interventions in at risk and healthy population. Clinical outcomes were reported in majority of the identified studies (51%), while humanistic and economic outcomes were reported less frequently. Our review found positive evidences of community pharmacy-based intervention in five chronic diseases. Further intervention in healthy and at risk population is strongly encouraged, particularly in cancer and mental illness. Humanistic and economic outcomes should also be measured to allow evaluating the holistic impact of community pharmacists' interventions.

Keywords: Community pharmacy, chronic disease, disease management, health promotion, prevention, pharmacy practice.

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INTRODUCTION

World Health Organization (WHO) defined chronic disease as diseases of long duration and generally slow progression[1]. As burden of disease globally, many chronic diseases such as cardiovascular disease and diabetes have already become leading causes of mortality[2]. Alarmingly, WHO forecasts the number of deaths due to the increasing number of patients with chronic diseases in the Western Pacific and South-East Asia regions[1]. Consequently, healthcare planners and professionals throughout the world are placing more emphasis on chronic disease management strategy[3]. However, a successful and sustainable disease management program requires a collaborative approach at the system level, with professional-directed and patient-oriented[4]. Conceptually, disease management is a comprehensive approach to prevent, and to manage the entire disease process. The aims of disease management are to improve clinical outcomes and quality of life. When properly implemented, disease management programs have demonstrated to facilitate improvements of clinical outcomes, and quality of life in patients as well as a reduction in management cost[5-9]. Among the healthcare professionals, community pharmacists are the most accessible and are in an ideal position to assist the management of patients with chronic diseases[10]. Recently, many developed countries such as United States (US), United Kingdom (UK) and Australia have expanded the roles of community pharmacists in cognitive services to provide a wide range of interventions[11-13]. With an increasing prevalence of chronic disease globally, there is an opportunity to further develop community pharmacists in professional healthcare delivery role in many countries. However, in order to take up the challenge, it would be necessary to examine what have already been done in chronic disease management by community pharmacists and the outcomes internationally to allow a successful adoption of the extended role.

Aim of the Review

The aim of this review was therefore to summarize and evaluate quantitative and qualitative evidence published in chronic disease management in community pharmacy internationally. We examined the interventions in the program identified and the effectiveness of the programs for five selected chronic diseases management in community pharmacy setting namely; cardiovascular disease (CVD), diabetes mellitus (DM), asthma, mental health, and cancer, which are identified as national health priorities in many countries[14, 15]. The results would provide valuable information for community pharmacists when planning services for chronic disease management.

MATERIALS AND METHOD

Search strategy

A literature search was performed covered the period from January 2000- March 2013 using EMBASE, Medline and International Pharmaceutical Abstracts (IPA).The limits were set to focus on research established since the implementation of the global strategy for health by WHO[16]. Search terms included: 'community pharmacy or pharmacists', 'pharmaceutical care', 'health promotion', 'intervention', 'prevention', 'screening', 'chronic disease', 'disease management', 'disease prevention' and 'health education'. Boolean operators were used to combine the search terms. No language restriction was applied for this search strategy. The bibliographies of included articles were searched manually to identify additional relevant studies for inclusion.

Inclusion and Exclusion criteria

All articles published in English were assessed initially for relevance based on titles and abstracts. Articles involving interventions carried out by community pharmacists were selected if they addressed one or more interventions and outcomes of the following conditions: cardiovascular disease, diabetes mellitus, asthma, mental illness and cancer, and/or reported economic outcomes of community pharmacy interventions, or reported sufficient information to allow an estimation of outcomes of the interventions or programs. Case reports, reviews, editorials, letters, and meeting abstracts were excluded.

Review methods

All duplicate articles were removed electronically (Endnote X2 software) and the remaining articles were screened by the reviewers to assess their eligibility according to the inclusion and exclusion criteria. Full copies of the potential eligible articles were obtained and each study was further reviewed independently by two reviewers. We treated multiple articles of results from the same study as a single program evaluation. Disagreements were resolved by another researcher not involved in the original review.

Classification of type of interventions

The interventions reported in the studies were classified based on disease management definition[4] as follows:

Patient-oriented (PO)

Education/ counselling (ED/C): Initial education and/or counselling session provided directly to patients (may include primary prevention, behaviour modification program).

Follow-up/monitoring (FU): Regular contact with patients (in person, by phone, by mail), and/or compliance monitoring

Risk screening (RS): Identify the people who are at risk of diseases or complications.

Professional Intervention (PI)

Medication review (MR): Identification of potential drug-related problems and/or recommendation made to physician.

Referral (RF): Patients referred to physician by pharmacists for further diagnosis and/or treatment.

Organization design (OD)

Practice guideline/disease management model (PG): The program or practice guideline designed or described by the organization of healthcare.

Classification of outcomes

Outcome measures assessed in the review included:

Clinical outcomes (disease controlled, pathology)

Humanistic outcomes (satisfaction and quality of life (QoL)) and

Economic outcomes (health care costs, cost-saving, and other related costs).

Quality assessment

Each study was graded using the evidence categories taken from the Department of Health in the National Service Framework, United Kingdom (17). The impact of the programs were determined as effective (i.e., when the outcomes showed significant difference, $p<0.05$) or not-effective.

RESULTS AND DISCUSSION

Study characteristics

Internationally, evidences for pharmacist involvement in disease management have increased in recent decades[74]. This review summarized different interventions provided by community pharmacists and its outcomes for the management of five chronic diseases internationally. Overall 2,973 articles were identified from the databases. After reviewing process based on the title of articles, abstracts, and content analysis, 82 studies were included in the final analysis (Figure 1). Twenty-eight identified studies were conducted in North America (United States and Canada), followed by 24 studies in United Kingdom and other European countries, 10 studies in Australia, 5 studies in Asia, 2 studies each in Turkey and New Zealand, 1 study each in Argentina, Brazil, Nigeria, and Chile. Overall, 35%, 34% and 24% of the retrieved articles

focused on community pharmacy interventions in cardiovascular disease, diabetes and asthma respectively; only 4% and 2% of retrieved articles focused on community pharmacy interventions in mental illness and cancer respectively. Approximately 44% of the retrieved articles were categorized as grade AI evidence (with the majority of the studies being in cardiovascular diseases and diabetes), followed by 28% and 26% of the studies graded BIIb and graded BIII respectively.

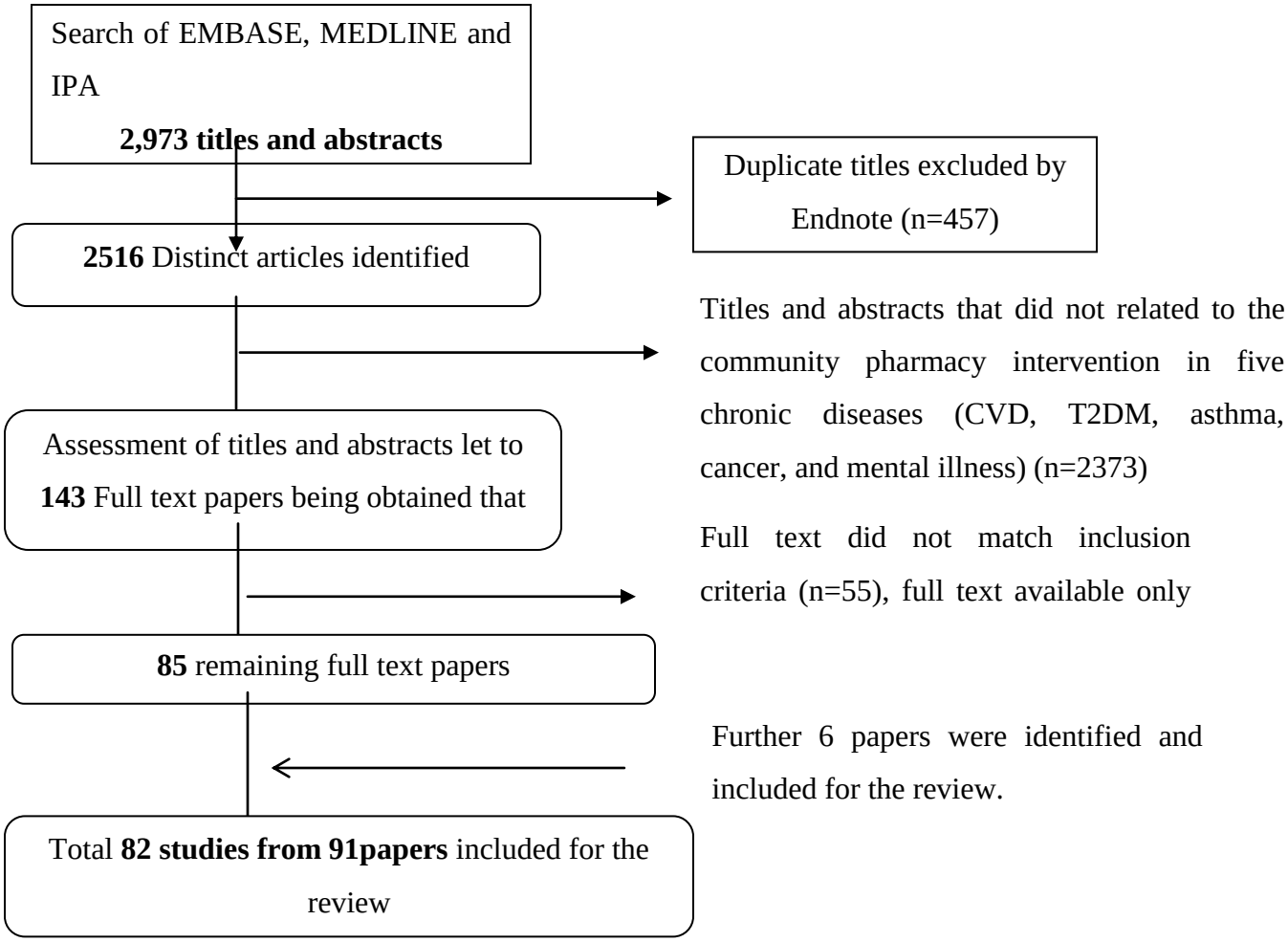

Figure.1. Flow diagram of literature search and review process

Type of interventions provided in community pharmacies and population characteristics

When coming to the type of interventions, our review showed that many different types of interventions were being implemented, with education and counselling being the most common intervention. In addition, many of the retrieved studies applied multiple interventions, possibly because multiple interventions are more likely to be successful than single intervention75. Approximately 53% of overall interventions from the identified studies described PO intervention, followed by 44% of a combination of PO and PI. The number of interventions

included in each disease management were varied, with 12 studies using single intervention, 38 using two interventions, 21 using three interventions, and no study using more than five interventions. Overall, education and counselling are the major type of interventions used for the five chronic diseases management included in this review (50%), followed by disease monitoring or follow up (18%), medication management (13%), referral (10%) and risk screening (6%) (Table1). Approximately 87% of identified studies reported interventions in populations with existing diseases. Only 6% and 7% of identified studies were intervention studies in at risk population and healthy population respectively (Table 1). Furthermore, the ratios of intervention studies performed in population with existing diseases to the intervention studies performed in at risk and healthy population have not changed during 2000-2012 (Figure 2).

Table 1: Type of interventions and population by diseases

Disease	Interventions					Population		
	Education and/or Counselling	Follow-up and/or Monitoring	Risk screening	Medication review or medication management	Referral	Healthy	At risk	Existing disease
CVD	29	8	9	7	9	6	3	20
Diabetes	33	15	2	13	7	0	2	26
Asthma	29	10	0	4	3	0	0	20
Mental illness	4	1	0	1	0	0	0	3
Cancer	1	0	1	0	1	0	0	2
Total	**96**	**34**	**12**	**25**	**20**	**6**	**5**	**71**

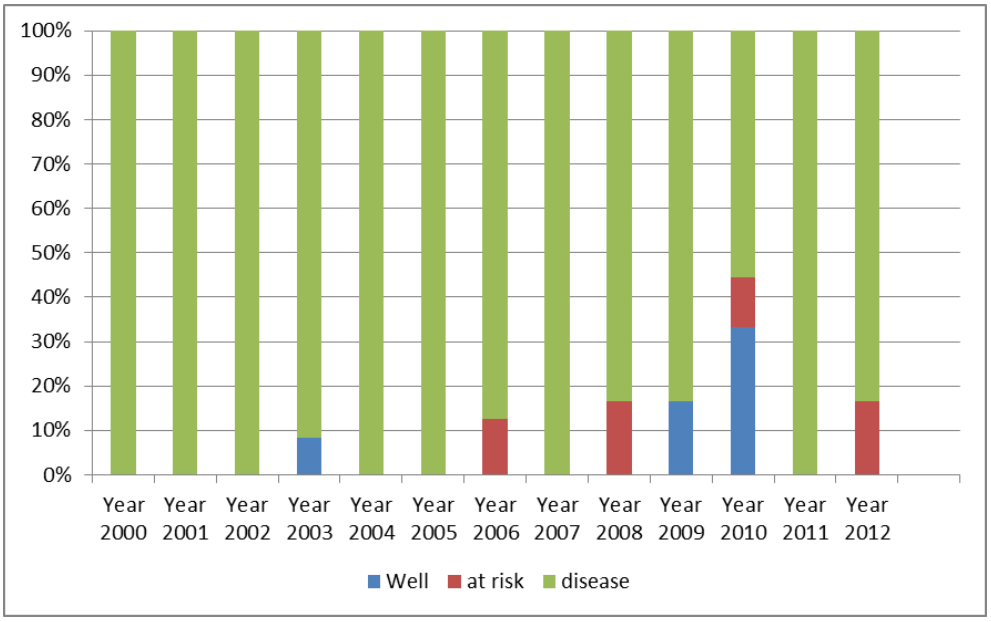

Figure 2: Percentage of intervention studies performed in established diseases, at risk and healthy population during the year 2000 – 2012 (n=82).

Outcomes

Key outcomes measures from the identified studies were primarily clinical or disease-specific outcomes, such as HbA1c or fasting blood glucose (FBG) for the outcome of diabetes management, blood pressure or lipid profile for the outcome of CVD management. Approximately 43% of total articles included in this review reported humanistic outcomes. QoL and patient satisfaction were the majority humanistic outcomes reported in the identified studies (18% and 13% respectively). Only 12% of identified studies measured clinical outcomes, humanistic outcomes and economic outcomes all together for determining the impact of the intervention program (Table 2). The economic outcomes from identified studies were reported in terms of willingness to pay (WTP), cost-effectiveness of the interventions, and cost saving. The effectiveness of the intervention programs were summarized and presented in Table 3. In addition, our review also showed an increasing trend of reporting economic outcomes after the year 2005 (Figure 3).

Table 2: Type of outcomes measures and the effectiveness by diseases

Disease	Clinical	Clinical+ humanistic	Clinical + economic	Clinical+ humanistic+ economic
Cardiovascular disease	15	9	2	3
Diabetes	18	4	3	3
Asthma	5	11	0	4
Mental illness	2	1	0	0
Cancer	2	0	0	0
Total	**42**	**25**	**5**	**10**

Table 3: Effectiveness of chronic disease management interventions provided by community pharmacy based on clinical, humanistic and economic outcomes.

Condition	Number of effective interventions*		
	Clinical	Humanistic	Economic
Cardiovascular disease	16/18	5/12	2/5
Diabetes	23/27	7/7	6/6
Asthma	18/18	11/15	5/5
Mental illness	2/3	0/1	0/0
Cancer	1/2	0/0	0/0

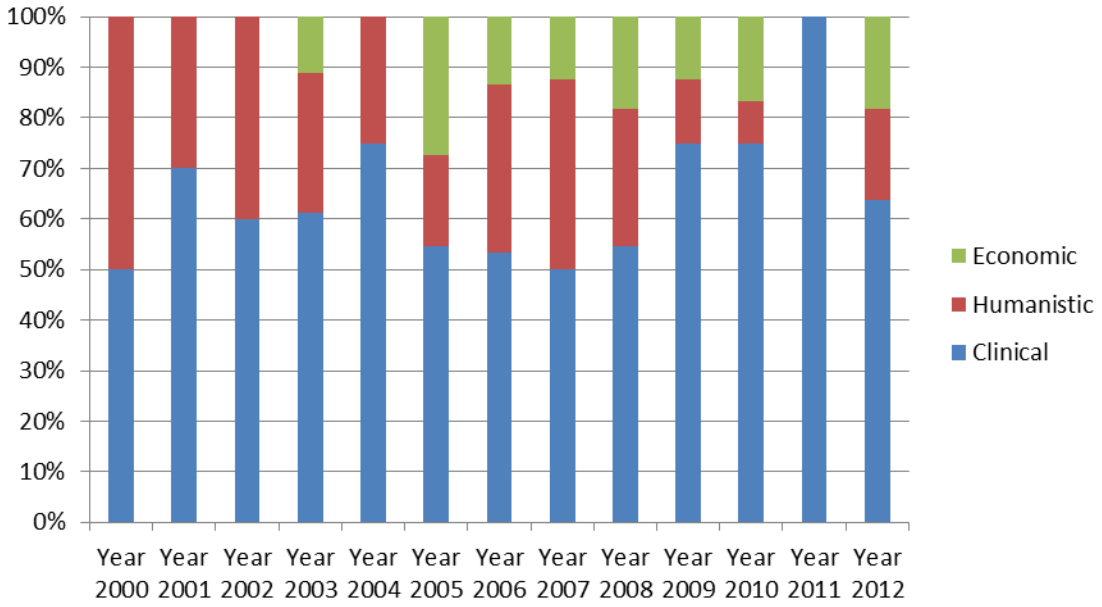

Figure 3: Percentage of clinical, humanistic and economic outcomes of the intervention studies reported in published studies during the year 2000 – 2012 (n=82)

Clinical effectiveness

The review found evidence of community pharmacy-based intervention in improving surrogate outcomes. Seven out of eight randomized controlled studies for diabetes management showed significant improvement in blood glucose level ($p<0.05$)[18-24]. Three out of nine randomized controlled studies in cardiovascular management showed significant improvement in blood pressure level ($p<0.05$)[25-28]. Similarly, other intervention studies also showed the positive outcome in reduction blood pressure level or improved lipid profile[29-39]. In addition, the outcomes from primary prevention by risk assessment resulted in finding high percentage (>50%) of individuals at risk of cardiovascular disease or diabetes, and the individuals were referred to the doctor for further medical investigation or diagnosis[40-48]. The studies of asthma management in this review showed evidence that patient education and scheduled counselling provided by community pharmacists resulted in improving asthma symptoms[49-61] and inhaler usage technique[62-64]. For the studies in mental illness, coaching by community pharmacists in antidepressant users showed improvement in depressive and anxiety symptoms, and medication adherence[65].

Humanistic effectiveness

Majority of humanistic outcomes reported in identified studies in this review were QoL and patient satisfaction. Evidence from randomized controlled studies included in this review reported improvement of QoL from the community pharmacists' intervention, but only 3 out of

25 studies showed significant improvement[24, 55, 56]. From the total of 35 studies reporting humanistic outcomes, 10 studies showed significant improvement of consumers' satisfaction level ($p<0.05$)[18, 35, 51, 57, 66] or high percentage (> 90%) of participants satisfied with the program[29, 36, 46, 67, 68].

Cost-effectiveness

Approximately 18% of studies included in this review reported economic outcomes. The evidence showed that intervention by community pharmacists resulted in reduction of healthcare cost[25, 58, 66, 67, 69, 70] and the programs appeared to be cost-effective[71-73]. Reported WTP values ranged from US$ 30-60 per consultation[29]. The details of the outcomes of the studies included in this review are presented in Table 4. For the five chronic diseases evaluated in the present review, majority of the studies reported pharmacist intervention in CVD, DM and asthma, with only limited number of studies reported involvement of community pharmacists in mental illness and cancer management. This finding may imply the lack of patient's awareness of the services that could be provided by community pharmacists about these diseases. Otherwise, this may reflect inadequate pharmacists' knowledge or ability in providing meaningful health care in those two diseases. However, a study did report the pharmacists believed that discussing cancer awareness was important and beneficial to patients[76]. Thus, further work is recommended to investigate barriers which prevent actualizing role in managing mental illness and cancer in community pharmacies. Mechanism such as training and education to enhance the role of pharmacist in these two diseases should be explored further. Practically speaking, disease management is a set of activities aimed at improving health outcomes such as disease prevention, risk management, diagnosis, and therapeutic monitoring[4]. Interestingly, only limited number of identified studies reported intervention in healthy and at risk population. This trend has not significantly changed in the past decade, even though WHO has encouraged the implementation of risk prevention policies internationally since 2002[77]. The finding from this review implies that community pharmacists are still not fully engaged to deliver health promotion advice and contribute to the disease prevention interventions at the present time. Admittedly, it is not a major role of pharmacist to diagnose chronic diseases. However, community pharmacist can be in a position to identify clients who are at risk and refer them for further diagnosis and management. In view that client had a positive attitude towards health services from community pharmacists and agreed that pharmacists are able to provide screening services for some chronic diseases[78], more pharmacists' intervention in healthy or high-risk population should be encouraged. Published studies have shown that prevention interventions in these groups of

population to reduce the risk factors will produce a substantial public health benefit[79, 80]. Another observation arising from the present review is the assessment of the effectiveness of community pharmacists' intervention. In the management of chronic diseases, clinical outcome may not always describe the aspect in the same way as HRQoL. Our present review showed positive impact of pharmacist intervention to the clinical outcomes, but limited number of studies showed program effectiveness on QoL and satisfaction level. In addition, our results also showed humanistic outcomes were under-performed internationally in the past decade. Likewise, economic or financial outcomes were also measured only by a small number of investigators[81, 82]. Due to an increasing constraint of healthcare resources globally, this outcome should be measured routinely to justify any extended roles of community pharmacists. Our current review also showed the increasing trend of the reporting of economic outcome in published studies after the year 2005. Thus, it would be feasible for the future intervention programs to quantitatively and qualitatively capture and evaluate the impact of pharmacists' intervention on all types of outcomes including clinical, humanistic and economic outcomes. This is of particularly importance in countries or jurisdictions where the practice of community pharmacy is less well developed. In our review, the majority of the studies identified were conducted in countries where the pharmacy profession is relatively well developed. Relatively small number of studies from developing countries was found, implying that few interventions were performed by community pharmacists in developing countries. Publication bias may need to be considered, as publications in languages other than English were excluded in this review. However, we are of the view that publication bias will have minimal influence (as less than 2% of total articles identified in the initial search were foreign language articles), but rather reflecting the real situation of a lack of a healthcare framework to engage community pharmacists in developing countries. In fact, most governments work closely with the community pharmacists within a well-designed framework in developed countries[83], whereas, the health systems in developing countries are different[84]. For instance, community pharmacies in the United States receive reimbursement for the implementation of Medication Therapy Management (MTM)[85], the Pharmacy Practice Incentives (PPI) program provides incentive payments to accredited community pharmacies in Australia to deliver cognitive services to improve patient outcomes [86]. Hence, investigation of the impact of the health care systems on providing chronic disease management services in community pharmacy is needed before implementing any large scale programs.

Table 4: Community pharmacy-based interventions and outcomes

Reference	Study design	Study population	Intervention	Outcomes measured			Evidence category
				Clinical	Humanistic	Economic	
Cardiovascular disease							
Ali,F et al.(F. Ali, Laurin, Lariviere, Tremblay, & Cloutier, 2003) 2003 (USA)	Cohort	149 patients prescribed with hypolipidemic medications	Education, telephone followed up program	Increase medical compliance ($p<0.05$), reduced total chol, TG, LDL ($p<0.001$, 0.01, 0.01 respectively)	99.2% satisfied with the program	Average WTP $34.50 per 30 min consultation	BIIb
Houle, SK et al.(Houle, Chuck, McAlister, & Tsuyuki, 2012) 2012 (Canada)	RCT	227 diabetes patients with high BP	Education, counselling, follow up, and referral	Reduction in SBP in intervention group from baseline compared to control group ($p=0.008$)	Not reported	Annual estimated cost savings from avoided cardiovascular events were $265/patient (95% confidence interval [CI] $63467)	AI
Liu,Y et al (Liu, McDonough, Carruthers, & Doucette, 2009) 2009 (USA)	Cross-sectional	265 union workers aged ≥ 20 years	Risk screening, education	51% had high SBP 25% had high DBP	Not reported	Not reported	BIII
Sookaneknun,P et al. (Sookaneknun et al., 2010) 2010	Cross-sectional RCT	456 people aged ≥ 40 706 angina,	Screening, referral	21.6% referred to GP, 0.4% diagnosed hypertension	Not reported No differences	Model unit cost for using Community	BIII AI

(Thailand) Bond,C.M. et al. (Bond et al., 2007) 2007 (UK)	Cohort	1308 hypertension patients aged < 65 years 100 hypertensive patients aged 18-80	Medication review, recommendation made to GPs. Education, BP monitoring	Greater proportion of the intervention group received fewer home visits for CVD-related reasons after the intervention (difference = 2.9% (95% CI: 0.7–5.4%). Reduction in SBP(p=0.01), DBP (p=0.28)	between the groups for any of the QoL measures employed. Improvement in vitality score (P=0.05), decline mental health score (p=0.01).	pharmacy =US$11.2/screened person. Total cost of pharmacist times £30/patient, higher total cost including pharmacist times in intervention group.	BIIb
Cote,I et al. (Cote, Gregoire, Moisan, Chabot, & Lacroix, 2003; Cote, Moisan, Chabot, & Gregoire, 2005) 2008 (Canada)	Cross-sectional	1130 clients aged 40-70 without known CVD	Risk assessment, counselling, referral	70% of clients referred to GP, 18% of clients had high CVD risk		Mean cost of pharmacist intervention $Can 30.68 per participant. WTP $Can 0.54/month Benefits were about ten times higher than costs.	BIII
Horgan, JM et al.(Horgan, Blenkinsopp, & McManus, 2009) 2010 (UK)	Cross-sectional	204 clients aged ≥ 18 years without known CVD	Risk assessment, counselling, referral	64% of clients are overweight, 30% required referral to GP	Not reported	Not reported	BIII
Hourihan,F et al.(Hourihan, Krass, & Chen, 2003) 2003 (Australia)							

					Not reported		
Lalonde,L et al.[Lalonde et al., 2006] 2006 (Canada)	RCT	42 patients aged 30-74 years	Counselling, education	Reported increase physical activity (88% of patients), reduction of dietary fat 54%, weight loss (33%).	No statistically significant differences in patient satisfaction with the decision-making process were detected between the study groups.	Not reported	AI
Mangum, SM et al.[Mangum, Kraenow, & Narducci, 2003] 2003 (USA)	Cross-sectional	351 clients aged ≥ 18 years visiting pharmacies	BP screening, referral	62% of clients had high BP, 36% referred to GP	Not reported	Not reported	BIII
Olenak, JL et al.[Olenak & Calpin, 2010] 2010 (USA)	Cross-sectional	239 clients aged ≥ 18 years with no history of CHD	Risk assessment, education	8.3% of participants screened were at high risk CVD	80% of participants rate the program as excellent	Not reported	BIII
Pongwecharak J et al.[Pongwecharak & Treeranurat, 2010] 2010 (Thailand)	Single group, pre and post-test	350 clients aged ≥ 35 years 217 patients	Screening, BP reading, BG testing, education Education, referral	36% pre-hypertensive, 29% hypertensive, 40% made lifestyle changes Pharmacologic risk reduction therapy was initiated or enhanced in 53.7%	Not reported Not reported	Not reported	BIIb
Semchuk,W							

et al[Semchuk et al., 2007) 2007 (Canada)							
Winfrey,C et al[Winfrey et al., 2011) 2011 (USA)	Cross-sectional	39 patients, aged > 50 years	PAD screening, counselling education, referral	44% of patients referred to GP, 23% detected with PAD	Not reported	Not reported	BIII
Nola, KM et al[Nola et al., 2000) 2000 (USA)	RCT	51 patients	Education, medication management	32% in intervention group achieved cholesterol goal (15% in control group)	Satisfaction scores intervention vs control (no significant)	Not reported	AI
Robinson,J et al[Robinson, Segal, Lopez, & Doty, 2010) 2010 (USA)	Cohort	276 hypertensive patients	Education, medication management	Reduction in SBP ($p<0.05$), DBP ($p=0.16$), improved medication adherence	Not reported	Not reported	BIIb
Zillich, AJ et al[Zillich, Sutherland, Kumbera, & Carter, 2005) 2005 (USA)	RCT	125 patients with uncontrolled BP	BP monitoring, education	Different reduction in SBP ($p<0.12$) and DBP ($p=0.03$) between groups	Not reported	Not reported	AI
Garcao, J et al (Garcao & Cabrita, 2002) 2002 (Portugal)	RCT	100 hypertensive patients 282	BP, DRP monitoring	Decreased prevalence of uncontrolled BP in intervention group ($p<0.0001$), 40% of	Increased satisfaction	Not reported	AI

		hypertensive patients	BP monitoring, counselling, referral	potential DRPs prevented Increased number of patients with controlled BP in intervention gr. ($p<0.05$)	level in intervention group ($p<0.05$)		
Blenkinsopp, A et al (Blenkinsopp, Phelan, Bourne, & Dakhil, 2000) 2000 (UK)	RCT	Dyslipidemic patients			Improved QoL	Not reported	AI
Paulos, CP et al.(Paulos, Nygren, Celedon, & Carcamo, 2005) 2005 (Chile)	RCT	899 Statin users aged ≥ 18 years	Education	Decreased cholesterol level[intervention = -27.1 mg/dl, $p=0.023$, control=-1.4mg/dl, $p=0.663$]	Not reported	Not reported	AI
Eussen, SR. et al. (Eussen et al., 2010)2010 (Netherland)	RCT	152 patients with heart failure.	Education, counselling	Lower rate of discontinuation (95% CI 0.46 to 0.96 for 6 month, 95% CI 0.65 to 1.10 for 1 yr.	No significant difference in disease specific HRQoL between groups	Not reported	AI
Bouvy, M et al(Bouvy et al., 2003) 2003 (Netherland)	Cohort	42 hypertensive patients	Counselling (monthly)	Medication non adherence in intervention =140/7656 days, control 337/6196 days, RR=0.32	Improved satisfaction rate ($p=0.013$)	Not reported	BIIb
Oparah, AC et al(Oparah, Adje, & Enato, 2006). 2006 (Nigeria)	Cohort	389 participants	Counselling, monitoring	Reduction in SBP,DBP ($p<0.0001$)	Consumers satisfied with the service	Not reported	BIIb
Krass,I et al(Ines Krass,	RCT		Screening, counselling		No change in QoL at 6 month after initial	Not reported.	AI

Hourihan, & Chen, 2003) 2003 (Australia)	RCT	293 patients with heart failure		Reduction in SBP (p=0.012), reduction in TC (p<0.003)	visit (p=0.08) Not reported	Not reported	AI
Holland, R et al(Holland et al., 2007) 2007 (UK)	Cohort	52 patients with diabetes and hypertension	Medication review, home-visit, education, counselling	Number hospital readmission (intervention=134, control=112, p=0.28)	Not reported	Not reported	BIIb
Planas, LG et al(Planas, Crosby, Mitchell, & Farmer, 2009) 2009 (USA)	Cohort	70 at-risk participants aged 50-74 years	Medication therapy management, follow-up	Mean SBP decreased (p=0.003),12.9 times than control group achieved goal BP (p=0.021), increased medication adherence (not significant difference)	Not reported	Not reported	BIIb
McNamara, KP et al(McNamara et al., 2012) 2012 (USA)	RCT	56 workers with risk factors of CVD	Risk management, education	Significant reduction in mean BP, waist circumference	Not reported	Not reported	AI
John, EJ et al(John et al., 2006) 2006 (USA)		150 participants with hypertension	Education, lifestyle and medicine management	Reduction in mean BP (p=0.016 for SBP, 0.019 for DBP)			
Pilar, ZF et al(Zaragoza-Fernández, Gastelurrutia, Cardero, &			Education, lifestyle modification	Intervention: reduction in SBP and DBP 16.08, 9.95 control: 1.79,0.95 (p<0.001)			

Martinez-Martinez, 2012) 2012 (Argentina)							
Diabetes Adepur, R et al(Adepu, Rasheed, & Nagavi, 2007) 2007 (India)	RCT	70 T2DM patients	Counselling, education	Blood glucose level decreased in test group ($p<0.05$)	Improvement in mean QoL ($p<0.05$)	Not reported	AI
Ali, M et al(M. Ali et al., 2012) 2012 (UK)	RCT	46 T2DM patients	Counselling, education, monitoring	Reductions in BMI (30.8 to 27 kg/m(2), $P < 0.001$) and blood glucose (8.8 to 6.9 mmol/l, $P < 0.001$) in intervention group	Increase satisfaction with the information received ($p<0.001$), no significant difference in diabetes related QoL.	Not reported	AI
Armour, C et al(C. L. Armour, Taylor, Hourihan, Smith, & Krass, 2004) 2004 (Australia)	RCT	188 patients with T2DM aged 18-85	Medication review, BG monitoring, counselling	Reduction in BG level ($P<0.01$), improved medication adherence	Improved WB-Q12 scores in intervention ($p=0.04$)	Not reported	AI
Cranor, CW et al(Cranor & Christensen, 2012) 2012 (USA)	Cohort	85 patients with diabetes	Education, counselling, monitoring, follow-up, referral	HbA1C improved($p=0.04$)	Patient satisfaction with pharmacy service improved ($p<0.01$)	29% decreased in non-diabetic cost, 16% decreased in all-diagnosis cost	BIIb
Doucette, WR et	RCT	78 patients with diabetes	Planning,	No significant reduction in HbA1c ($p=0.27$),	Not reported	Not reported	AI

al(Doucette, Witry, Farris, & McDonough, 2009)			monitoring, follow-up, education, drug recommendation to GP	increased diet self-care activities (days) (p=0.001)			
2009 (USA)	Single group, pre and post-test	914 patients with diabetes		HbA1C decreased(p=0.002)	95.7% reported satisfied with pharmacy service	Reduced health care cost $1079/patient/ year	BIIb
Fera, T et al(Fera, Bluml, Ellis, Schaller, & Garrett, 2008)		103 patients aged ≥ 18 years with HbA1c ≥ 9.0%	Scheduled consultation, monitoring				AI
2009 (USA)	RCT					Not reported	
Jameson, JP et al(Jameson & Baty, 2010)			Medication management, education	Median A1C decrease of 1.50% (intervention group), 0.40% (control group) P =0.06	Not reported		
2010 (USA)	RCT	338 patients with T2DM aged 45-75					AI
				Reduced HbA1C (p=0.009)	Not reported	Not reported	
Mehuys, E et al(Mehuys, De Bolle, et al., 2008)			Education				
2008 (Belgium)	Cohort	25 patients with T2DM					BIIb
					Not reported	Not reported	
Ozkam, M et al(Ozkan & Ozcelikay, 2012)			Education	Increased percentage of patients engaged in regularly lifestyle (32% → 48%)			
2012 (Turkey)	Cohort	349 aged ≥ 18 diagnosed with T2DM			Not reported	Not reported	BIIb
Rothman,R et al(Rothman, Malone, Bryant, Horlen, & Pignone,			Medication management, education, follow-up, treatment recommendation	Reduction in HbA1c (p<0.0001)			
	Single group,	137 patients with T2DM					BIIb
					Not reported	Not reported	

2003) 2003 (USA)	Longitudinal	99 patients with T2DM aged < 85 years	Medication management, education, follow-up	Improved FBS(p=0.004)	Not reported	Cost to healthcare sector,$383/patient/9 month for each 1% reduction in HbA1c.	AI
Sansgiry, SS et al(Sansgiry et al., 2012) 2012 (USA)	RCT	191 patients with diabetes	Medication review, BG monitoring, follow-up, education, counselling	Decreased HbA1c 0.46% from baseline (p=0.02)	Not reported	Based on an estimated savings of $820 for each 1% decrease in A1C, cost avoidance was calculated as $59,040	BIII
Taylor, SJ et al(Taylor et al., 2005) 2005 (Australia)	Cohort	1370 person aged ≥ 18 years with BMI ≥ 25 + ≥ 1 risk factor	Medication management, education, referral	Change in HbA1C -1.7%, p<0.05	Not reported	Not reported	BIII
Ragucci, KR et al(Ragucci, Fermo, Wessell, & Chumney, 2005) 2005 (USA)	Single group, longitudinal		Risk assessment, counselling, referral	Reduction in BMI and body weight (p<0.001)			
Botomino, A et al(Botomino, Bruppacher, Krahenbuhl, & Hersberger, 2008) 2008 (Switzerland)	CT	161 patients with T2DM, aged ≥ 30	Medication management, regimen intervention, education	Reduced HbA1c (p<0.001), FBS (p=0.02)	Not reported	Not reported	BIIa
Correr, CJ et al(Correr,	RCT	112 patients with diabetes			Not reported	Not reported	AI

Melchiors, Fernandez-Llimos, & Pontarolo, 2011) 2011 (Brazil)		72 patients with diabetes	Medication management (detection and resolution of DRPs), education, intervention with GPs	Reduced HbA1c (p<0.0001), FBS (p=0.0004), Increase knowledge about the disease (P<0.001)	Not reported	Not reported	BIII
Fornos, JA et al(Fornos, Andres, Andres, Guerra, & Egea, 2006) 2006 (Spain)	Cross-sectional	289 patients with T2DM		22% of clients diagnosed of DR, increased knowledge about the disease (no significant value provided)	Increased health-state scale (p=0.02), no significant change in utility scores	Not reported	AI
Jimenez, FJ et al(Jimenez-Ramirez & Perez, 2011) 2011 (Puerto Rico)	RCT	478 patients with diabetes	Diabetes complication screening, education		Not reported	Not reported	BIII
Krass, I et al(I. Krass et al., 2007) 2007 (Australia)	Cohort	54 patients aged ≥ 18 years with T2DM		Blood glucose level decreased (p<0.01)	Not reported	Not reported	BIII
Muller, U et al(Muller, Hammerlein, Casper, & Schulz, 2006) 2006 (Germany)	Cross-sectional	126 patients with T2DM	SMBG monitoring, education, medication review	SMBG errors reduced (p=0.001)	Not reported	Not reported	BIIb
Nau, DP et al(Nau, Blevins, & Neal, 2001) 2001	Cohort Single group,	24 patients with T2DM aged 31-75 years	Education Clinical assessments, follow-up Education, BG monitoring, clinical	64% of patients not achieved therapeutic goals Reduction in FBS (p=0.001)	Not reported Improved QoL by 5%	Cost benefit ratio is at least 1:1	BIIb

(USA) Oyetayo, OO et al[Oyetayo, James, Martinez, Roberson, & Talbert, 2011) 2011 (USA)	longitudinal CT	22 patients with T2DM	assessment, drug therapy management with physicians		Not reported	Decrease medical costs (p=0.003), saving of $35,511 from baseline	BIIa
		67 patients with T2DM, aged ≥ 18 years	Education	Reduction in FBS (p<0.05)		Not reported	BIIb
Petkova, VB[Petkova & Petrova, 2006) et al 2006 (Bulgaria)	Single group, longitudinal	62 patients with T2DM	Education, monitoring	Reduction in HbA1c (p<0.001)	Not reported	Not reported	BIIb
Rashed, SM et al[Rashed, Goldstein, Tolley, & Wilson-Relyea, 2010) 2010 (USA)	Single group, longitudinal	30 patients with diabetes	Counselling, BG and BP monitoring	Number of patient reached BG goal increased from 16.3% to 39.5%, reduction in mean body weight and BMI (p<0.01)	Not reported	Not reported	BIIb
Turnacilar, M et al[Turnacilar et al., 2009) 2009 (Turkey)	Retrospective, non-experimental	198 patients with diabetes	Counselling, drug therapy management, monitoring	Reduction in HbA1c (p<0.05), improved knowledge about oral-hypoglycemic drugs (p=0.002)	Not reported	Not reported	AI
Wermeille, J et al[Wermeille, Bennie, Brown, &							

McKnight, 2004)					Not reported		
2004 (UK)	RCT	77 patients with T2DM	Education	Reduction in HbA1c, increased number of patients perform daily foot exam, monitor glucose daily (p=0.0005), and regularly exercise (30 min) (p=0.007)	Not reported	Not reported	AI
West, D et al(West, Blevins, Brech, Stotts, & Gardner, 2003) 2003 (USA)	RCT	396 patients with asthma, aged 18-75 years	Education, counselling, monitoring	Reduction in HbA1C (p=0.04)	Improvement QoL(p=0.05) and asthma knowledge (p<0.01)	Costs per QALY gained of AUS$4753	AI
Clifford, RM et al(Clifford, Davis, Batty, & Davis, 2005) 2005(USA)	RCT	201 patients (94 control, 107 intervention)	Education, medication management	Reduction in HbA1C by 0.4% at 24 months after baseline (p=0.023)			AI
Sarkadi, A et al(Sarkadi & Rosenqvist, 2004) 2004 (Sweden)	RCT	50 individuals with mild asthma, aged 18-40 years)	Clinical assessment, monitoring	Improved asthma control from "severe" to "not severe" in intervention than control patients (p<0.001)	No significant difference in asthma QoL Improved asthma QoL, satisfaction.	Not reported Not reported	AI
Asthma Armour, C et al(C. Armour et al., 2007) , Gordoris,A et al(Gordois et al.,	RCT	90 patients with asthma (51-intervention, 39 control)		Increased asthma control score (p=0.038)	Improved asthma QoL at 4 months after	Cost saving = A$5632.7/month	AI

2007), 2007 (Australia)			Education, scheduled counselling		initial visit (P=0.02), no significant difference between intervention and control (p=0.1)		AI
Mehuys, E et al(Mehuys, Van Bortel, et al., 2008) 2008 (Belgium)	RCT	106 asthma patients	Education, monitoring	Asthma symptoms improved, decreased hospitalization rate	Not reported	Not reported	BIII
Petkova, VB et al(Petkova, 2008) 2008 (Bulgaria)	Cohort	28 asthma patients	Education, counselling, monitoring	Reduction in asthma severity score, risk of non-adherence (p<0.001)	89.3% of patients satisfied with the service	Not reported	AI
Saini, B et al(Saini et al., 2008) 2008 (Australia)	RCT	24 asthma patients aged 18-65 years	Education	Improvement in inhaler usage technique, medication adherence (p<0.05)	Not reported	Not reported	BIII
Kumar, A et al(Kumar, Adepu, Parthasarathi, & Mahesh, 2009) 2009 (India)	Cohort	1551 asthma patients (702-intervention, 849-control)	Education, scheduled counselling	50% of patients reported problems solved	Not reported	Not reported	BIIb
Naerhi, U et al(Narhi, Airaksinen, &	Cohort	4080 asthma patients 100 asthma patients	Education, counselling,	Improved symptoms score (p<0.001) Improved preventer-to-	Not reported	Not reported	BIIb

Enlund, 2002) 2002 (Finland)		757 patients with asthma or COPD	weekly-follow up Education, follow-up	reliever (P:R) ratio (p<0.001)	Improved asthma QoL (p=0.12)	Not reported	
Barbanel, D et al(Barbanel, Eldridge, & Griffiths, 2003) 2003 (UK)	Single group, longitudinal	91 asthma patients (35 intervention, 56 control)		Decreased nocturnal awakening (p<0.05), 72% went to the doctor for reassessment	Not reported	Not reported	AI
Bereznicki, B et al(Bereznicki, Peterson, Jackson, Walters, & Gee, 2011) 2011 (Australia)	RCT	161 (intervention), 81 (control) asthma patients	Education, counselling, referral	75% of patients, improved asthma symptoms	Improved asthma QoL score (p<0.01), intervention group showed greater scores (p<0.01)	Not reported	BIIa
Diamond, SA et al(Diamond & Chapman, 2001) 2001 (Canada)	CT	214 asthma patients	Education, monthly counselling	Reduced percentage of patients perform mistake in inhalation techniques (78.9% vs 28.3%)	Improved asthma QoL score (p<0.005)	Unit cost per patient enhanced care=$150 Usual care =$315	AI
Emmerton, L et al(Emmerton, Shaw, & Kheir, 2003) 2003 (New Zealand)	RCT	1113 patients with COPD or asthma	Education	Improved asthma control score both intervention and control (p=0.03 and p=0.01 respectively) ,no difference between groups	Improved asthma related QoL (p=0.0001)	Not reported	AI
Hammerlain, A et al(Hammerlein, Muller, & Schulz,	RCT	207 patients with asthma	Education, goal-setting, medication management	Increased FEV1 (p=0.475, between	More satisfied in pharmaceutical care group (p=0.03), improved H RQoL in both groups	Direct cost savings averaged 725 dollars/patient/year, and indirect cost	BIIb BIII

2010) 2010 (Germany)	Single group, pre and post-test	183 asthma patients, aged 18-65 years	Education, medication management	groups), improved inhalation technique (p=0.001)	(no significant difference)	savings were estimated to be 1230 dollars/patient/year.	
Odedina, FT et al(Odedina, Leader, Venkataraman, Cole, & Storm, 2000) 2000 (Australia)	Cohort	500 asthma patients aged 16-60 years	Education, counselling, monitoring, referral	Increased PEFR (p=0.0002)	Increased proportion of patients with asthma action plan	Insurance claimed data revealed better adherence to evidence-based therapy	BIIa
Schulz, M et al(Schulz et al., 2001) 2001 (Germany)	CT	62 asthma patients, aged ≥ 17 years	Education, counselling, monitoring	Increased PEFR from baseline in both groups (p<0.01), higher peak flow rate in intervention group (p-0.02)	Increased asthma knowledge, improved asthma HRQoL(p<0.001)	Not reported	BIII
McLean, W et al(McLean, Gillis, & Waller, 2003) 2003 (Canada)	Cohort	48 asthma patients	Education, scheduled consultation, follow-up, referral	Improved asthma severity (p<0.008)	Increased HRQoL(p=0.002), satisfaction (p=0.119)	Not reported	AI
Weinberger, M et al(Weinberger et al., 2002) 2002 (USA)	RCT		Education, monitoring	Decreased asthma severity (p<0.002)	Improved asthma related QoL (p=0.01)		
Bunting, BA			Medication management	Change in medication used and improved asthma treatment, decreased asthma symptoms (p<0.022) 4.3 DRPs per patient	100% of participants indicated that they have satisfied with the program		

et al[Bunting & Cranor, 2006] 2006 (USA) Mangiapane, S et al[Mangiapane et al., 2005] 2005 (Germany) Herborg, H et al[Herborg et al., 2001] 2001 (Denmark) Kheir, N et al[Khier, Emmerton, & Shaw, 2001] 2001 (New Zealand) Kritikos, V et al[Kritikos, Armour, & Bosnic-Anticevich, 2007] 2007 (Australia)			Counselling, education, monitoring, medication management, follow-up Education, counselling	were detected Decreased proportion of patients with severe asthma in intervention ($p<0.05$)			
Mental illness Crockett, J et	RCT	106 patients, aged ≥ 46	Counselling	Adherence to medications was high in	Improved well-being score in both group	Not reported	AI

al[Crockett, Taylor, Grabham, & Stanford, 2006) 2006 (Australia) Ewan, MA et al[Ewan & Greene, 2001) 2001 (UK) Brook, O et al[Brook, Van Hout, Nieuwenhuysea, & De Haan, 2003) 2003 (Netherland)	Single group, longitudinal RCT	years 38 mental illness patients 151 patients who attended pharmacy for non-TCAs	Medication management, education, counselling Counselling, monitoring	both groups 91% of patients had appropriate intervention Intervention patients were less depress and anxious ($p<0.05$)	Not reported Not reported	Not reported Not reported	BIII AI
Cancer Giles, JT et al[Giles et al., 2001) 2001 (USA) McGuire, TR et al[McGuire, Leypoldt, Narducci, & Ward, 2007) 2007 (USA)	Cohort Cross-sectional	140 women aged ≥ 18 years 300 participants	Risk screening, education Referral	Increased self-assessment rate (31% to 56%) after intervention 37% referred to GP	Not reported Not reported	Not reported Not reported	BIII BIII

Limitations

Our review has several limitations. Firstly, our review focused only on indexed English literature from Embase, Medline and IPA database. Thus, unpublished literature or published literature from other databases and non-English studies may not have been included. Secondly, we only focussed on the studies in the nominated five chronic diseases, and may have missed out interventions in other chronic diseases. Thirdly, there was no direct comparison between different interventions; this may limit to evaluate the interventions' relative effectiveness. Lastly, it is possible that successful intervention programs are more likely to be published, and may contribute to publication bias. However, currently, there is no perfect method to ascertain this. Nevertheless, we believe our manuscript can provide crucial information on the existing role of community pharmacists for chronic diseases management in recent decade, which would potentially assist in planning healthcare strategies in the future.

CONCLUSION

The current review highlights the positive outcomes of community pharmacy interventions in five chronic disease categories, but the major focus of intervention are in patients with existing diseases. Community pharmacists should be encouraged to implement proactive interventions for the general or at risk population, and particularly for mental illness and cancer. Furthermore, the relative cost-effectiveness associated with different interventions and factors impacting the successful implementing such interventions at community pharmacy still need further determination.

Conflict of Interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the manuscript.

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