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A systematic review and meta-analysis of pharmacy education and practice on prevention and management of noncommunicable diseases in ASEAN countries

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Noncommunicable diseases (NCDs) are the leading cause of morbidity and mortality in ASEAN countries. However, consolidated evidence regarding the effectiveness of pharmacy practice interventions in ASEAN is still unclear. This study aimed to explore the scope and impact of pharmacy practice in managing NCDs in ASEAN countries. Systematic searches were conducted in 12 databases (PubMed™, Science Direct™, Scopus™, Springer Link™, Web of Science™, Cochrane Library™, and other databases) for studies published between 2001 and 2021. Of the 171 included studies from seven countries, seven focused on pharmacy education and showed improvements in students' knowledge and skills. Meta-analyses were performed on 47 randomized controlled trials using a random-effects models and risk of bias assessment. Pharmacists' interventions significantly improved fasting blood glucose, HbA1c, lipid parameters, blood pressure, and percent peak expiratory flow rates, compared to usual care. No significant improvements were found in blood pressure (particularly in diabetes subgroups), smoking cessation, or body weight. Positive humanistic outcomes, such as patient satisfaction, knowledge, and quality of life, were reported. While the studies in the meta-analyses were limited to Thailand, Malaysia, Indonesia, and Lao PDR, pharmacists' practice interventions in ASEAN countries demonstrated positive impacts on both clinical and humanistic outcomes. Due to a high overall risk of bias, the results should be interpreted with considerable caution. Further large-scale, long-term, and rigorous studies should be undertaken.

Systematic review registration: The Prospective Registration of Systematic Review on April 10, 2022, https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=316184.

Keywords Pharmacy practice, Pharmacy education, Noncommunicable disease, Meta-analysis, Systematic review, ASEAN

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Noncommunicable diseases (NCDs) are the major cause of death worldwide. NCDs kill 41 million people per year, equivalent to 71% of all global deaths[1]. Multiple NCDs covering cardiovascular disease (CVD), cancers, diabetes, and chronic obstructive pulmonary disease share common lifestyle-related risk factors such as poor diet, physical inactivity and tobacco consumption[2]. These four NCDs contribute to approximately 57% of global mortality[1]. Cardiometabolic diseases such as metabolic syndrome, prediabetes, prehypertension, and dyslipidemia, involve insulin resistance which plays a key role in accelerating atherogenesis[3]. Chronic respiratory diseases, especially chronic obstructive pulmonary disease (COPD), characterized by persistent low-grade systemic inflammation, are also associated with atherosclerosis, an important risk factor for cardiovascular morbidity and mortality[4].

Of all NCD deaths, 77% are in low- and middle-income countries[1]. The burden of NCDs among adults is rapidly increasing in the Asia-Pacific region, including Association of Southeast Asia Nations (ASEAN) countries. In the age group of 15 to 59, chronic NCDs accounted for 51% of deaths in ASEAN countries[5]. The top risk factor for disability adjusted life years in males is tobacco use and in females high fasting plasma glucose[6]. In ASEAN, nearly 20% of the adults are current smokers, ranging from 10% in Singapore to 28.9% in Indonesia, contributing to 10% of the global adult smoker population[7]. Tobacco smoking is responsible for 10.8% of all-cause mortality across the region, with approximately 526,000 deaths annually. Mortality rates attributable to smoking vary widely from 68.9 per 100,000 males in Singapore to 364 per 100,000 males in Cambodia[8]. In diabetes patients, the prevalence of hypertension exceeds 70%, with rates particularly high in Thailand (ranging from 80.5 to 89.3%). Moreover, most studies report that fewer than 50% of these patients achieve target glucose control[9].

Sustainable Development Goal (SDG) target 3.4 aims to reduce premature mortality from NCDs by a third by 2030. Country-specific decisions on interventions are required, including increased tobacco control and effective health system interventions, which will reduce NCD causes of death to achieve SDG target 3.4[10]. The interventions cover hypertension and diabetes treatment; primary and secondary cardiovascular disease prevention in high-risk individuals; treatment of acute cardiovascular diseases, diabetes complications, and exacerbations of asthma and COPD; and effective cancer screening and treatment[10].

The management of NCDs and other clinical conditions related to NCDs is complicated and resource consuming. Therefore, primary prevention strategies, including the modification of risk factors, are guided by established guidelines[11–13]. Several studies have shown that pharmacists' involvement as primary care providers help fill gaps in the primary prevention of NCDs, particularly by modifying risk factors. Pharmacists' contributions, including collaborative practices with physicians, have demonstrated improved control of cardiovascular disease (CVD) risk factors[14,15], diabetes[16], hemoglobin A1c (HbA1c)[17], systolic blood pressure[17,18], low-density lipoprotein cholesterol (LDL-C)[15,19] and medication adherence[16].

Collaborative practice agreements (CPAs) were initiated in the United States to permit pharmacist responsibility for a variety of functions, including patient assessment; ordering drug therapy and related laboratory tests; and selecting, initiating, monitoring, continuing and adjusting drug regimens[20]. In 2019, the International Pharmaceutical Federation (FIP) reviewed the impact of pharmacists' interventions on prevention, screening, referral, therapy and disease management in CVD, diabetes, asthma, COPD, and cancer[21]. Later in 2022, FIP published a management of NCDs regulatory self-assessment and development tool for transforming pharmacy practice to support pharmacists ordering and interpreting point-of-care tests, and initiating, continuing and adjusting treatment[22].

The ASEAN region has limited technology, healthcare workforces and medicines for prevention and management of NCDs[23]. There are wide variations in pharmacy practice in ASEAN countries. The levels of acceptance of pharmacists' provision of patient care range from pharmacists being well accepted to complete lack of recognition by other health care professionals[24]. The limited career paths for pharmacists to provide care for patients with NCDs has been addressed among seven ASEAN countries[24]. Nevertheless, there is still limited knowledge of the current impact of pharmacy practice, including primary prevention strategies and pharmaceutical care, on NCDs and related clinical conditions in ASEAN countries. The aim of this systematic review was to explore the scope of pharmacy practice concerning NCDs and, where appropriate, perform meta-analyses to further assess the data obtained.

Materials and methods

This meta-analysis followed the extension to the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) checklist[25] (Supplementary Table S1).

Literature search

Fourteen database searches were planned, but two searches could not be performed (local libraries in Philippines, and Malaysia). Thus, a total of 12 databases (PubMed™, Science Direct™, Scopus™, Springer Link™, Web of Science™, Cochrane Library™, Google Scholar™, Thailis™, University of Health Science Lao PDR database™, Haiphong University of Medicine and Pharmacy (HPMU) database™, Sanata Dharma University (SDU) database™, and University Brunei Darussalam (UBD) database™) were searched without filters for studies published from January 1, 2001, to December 31, 2021. A Population, Intervention, Comparator, and Outcome (PICO) framework was used to guide the study inclusion criteria. The study population included research related to pharmacy education and practice in the primary prevention and management of NCDs in ASEAN countries. The interventions examined were methods used to provide primary and secondary prevention as well as treatments for NCDs. When applicable, interventions were compared to usual care. Outcomes accessed included student-related outcomes, as well as clinical, humanistic, and economic outcomes. Search terms were developed based on multiple resources[11–13], and were piloted and reviewed by researchers. NCDs were defined to cover three groups: first, diseases of cancer, stroke, myocardial infarction, cardiovascular diseases, COPD, asthma, and diabetes mellitus (DM);[11–13] second, risk factors including smoking, obesity, alcohol, sedentary behavior, hypertension, dyslipidemia, insulin resistance, food habits, overweight, depression, and anxiety;[11–13] and third, management of NCD clinical conditions such as chronic kidney disease, heart failure, sleep disorders, substance disorders, psychotic disorders, non-alcoholic fatty liver, and cancers were considered[11–13]. Search terms are shown in Table 1 and search strategies are presented in Supplementary Tables S2.1-S2.6.

Study selection and eligibility

This review included published and unpublished studies performed in ASEAN countries that evaluated interventions or activities, including in-class teaching, community teaching, interprofessional education, and pharmacy practice that were related to primary prevention and management of NCDs. Reports, reviews, news, letters to editor, study protocols that were not empirical studies, and studies published or conducted before 2001 or after 2021 were excluded. The included studies were performed by pharmacy students, teachers, and pharmacists. If there was a duplication of results between a thesis/research project/hard copy and a research publication, the research publication was used in the study. Nevertheless, the results from theses/research reports/hard copies were also used to extract other unpublished literature.

One researcher performed an initial search conducted on PubMed™ to identify relevant sources on the topic. The search strategies were slightly modified to meet the specific requirements of each database by 11 researchers (PSO, TBK, TS, CHS, SW, DTL, PS, NK, SS, JK, CP). In the first round, eleven researchers independently screened studies for relevance against the predetermined eligibility criteria. Three virtual meetings of the research team were held to discuss performing searches and screening of all titles and abstracts. For the second round, one researcher, (PSO), conducted a double-check of all the screened studies. Any disagreements arising between two authors during the selection were resolved by discussion, or by consulting the research group via email for their opinion. Search results from each database were entered in EndNote 20™ to check for duplication. Microsoft Excel™ (Microsoft Office Professional Plus 2019) was used on a Google™ drive for input of search results. Full texts were retrieved through institution registration and using a service from the MSU Academic Resource Center, Mahasarakham University, Thailand.

Data extraction and synthesis

Nine authors (TBK, TS, CHS, SW, DTL, PS, SS, CP, PSO) independently extracted the data from the studies. Then one researcher (PSO) reviewed all the extracted data against the reports. Any disagreements arising between two authors were solved by discussion. Before data extraction, quality assessment was performed by two screening questions from the Mixed Methods Appraisal Tool (MMAT)[26] (Table S3). Data extracted were first author's name, country, year of publication, study location, study design, interventions, time and duration, number of participants and study population characteristics, instruments, and results.

Clinical outcomes were explored. Meta-analyses were conducted when included studies were randomized controlled trials (RCTs). Data were pooled using a random-effects model. The proportions for outcomes

Group 1 MeSH term NCD	Group 2 primary prevention: risk factors	Group 3: primary prevention: clinical conditions	Group 4 pharmacy education and practice	Group 5 countries
Cancer (free text) OR	Smoking OR	Chronic kidney disease OR	Pharmacy education OR	Thailand OR
Stroke OR	Obesity OR	Heart failure OR	Pharmacy students OR	Singapore OR
myocardial infarction OR	Alcohol OR Alcohol drinking OR	HIV OR	Multidisciplinary team (free text) OR	Malaysia OR
cardiovascular diseases OR	Exercise OR	Sleep disorder (free text) OR	Community teaching (free text) OR	Brunei OR
chronic obstructive pulmonary disease OR	Hypertension OR	Substance disorder (free text) OR	Pharmacy practice (free text) OR	Philippines OR
diabetes mellitus OR	Dyslipidemias OR	Mood disorders OR	Pharmaceutical care (free text) OR	Indonesia OR
Asthma	Food habits OR diet habit OR dietary habit OR eating behavior OR	Psychotic disorders OR	Counselling OR	Vietnam OR
	Overweight OR	non-alcoholic fatty liver disease OR	Home visit OR	Laos, Lao PDR OR
	Insulin resistance OR	Hospital oncology service OR	Free text: Ppharmacy service OR community pharmacy OR hospital pharmacy OR	Cambodia OR
	Cholesterol OR		Medication therapy management OR	Myanmar OR
	Depression OR			ASEAN OR
	Anxiety OR			Southeast Asia
	Metabolic syndrome OR			
	Primary prevention OR			
	Sedentary behavior OR			
	Diet OR			
	Cardiovascular risk factor OR			
	Fats OR			
	Compliance			

Table 1. Search terms and strategies.

measures such as achieving in fasting blood glucose (FBG) or HbA1C were reported and estimated using relative risk (RR) with 95% confidence intervals (95%CIs). For mean values of outcomes measured by the same tool (e.g., FBG), those outcomes were combined and presented as weighted mean differences (WMD) and their 95%CIs.

Funnel plot tests for publication bias or small study effects were conducted in STATA™ version 15.0, using Begg's and Egger's test ($p < 0.05$ indicated a significant difference of publication bias or small study effects)[27]. Statistical heterogeneity among the studies was assessed using the chi-squared test ($p < 0.05$ indicated significant heterogeneity) and I^2 (0%-25%, low; ≥25%-74%, substantial; and ≥ 75%, considerable heterogeneity)[28]. Potential sources of heterogeneity were investigated by exploring its reasons with subgroup analyses.

Pre-specified subgroup analyses were performed based on the different types of pharmacists' interventions and diseases, since individual diseases used different tools for specific outcomes. In addition, sensitivity analyses excluding small-sample-size studies (to address small-study bias), and the theses (which accounted for nearly 40% of the included studies) were also conducted.

Quality assessment

Quality assessment was conducted using different tools based on the design. The Mixed Methods Appraisal Tool (MMAT) was applied to qualitative, quantitative randomized controlled trials, quantitative non-randomized, and quantitative descriptive studies. For economic evaluations, the Critical Appraisal Skills Programme (CASP) checklist was used to assess the risk of bias (for more information, see Supplemental Materials).

Risk of bias of the included RCTs was assessed by using ROB™ version 2.0 (ROB 2)[29]. Each domain was assessed and categorized into low risk, high risk, or unclear risk of bias. Risk of bias assessments were performed by two reviewers (PSO, CP). Any disagreements were resolved by discussion or by involving a third reviewer (RS) until consensus was reached.

Results

Search results and study selection

The searches in all databases resulted in a total of 15,504 titles: 5,303 from international databases and 10,201 from other methods. After title and abstract screening, 322 studies were explored further by reading the full text. Excluded studies are reported in Supplementary Table S2.7. Of 171 included studies, 47 were RCTs and used for meta-analyses as shown in Fig. 1.

Study characteristics

The characteristics of 171 included studies are presented in Supplementary Table S4. The studies were conducted in seven countries between 2001 and 2021, especially in Thailand, Indonesia, and Malaysia (Supplementary Fig S1 and Fig S2). Pharmacists' interventions were implemented across major NCDs, with the highest proportion in diabetes (34.5%). NCD risk factor interventions were delivered in six groups, most commonly hypertension

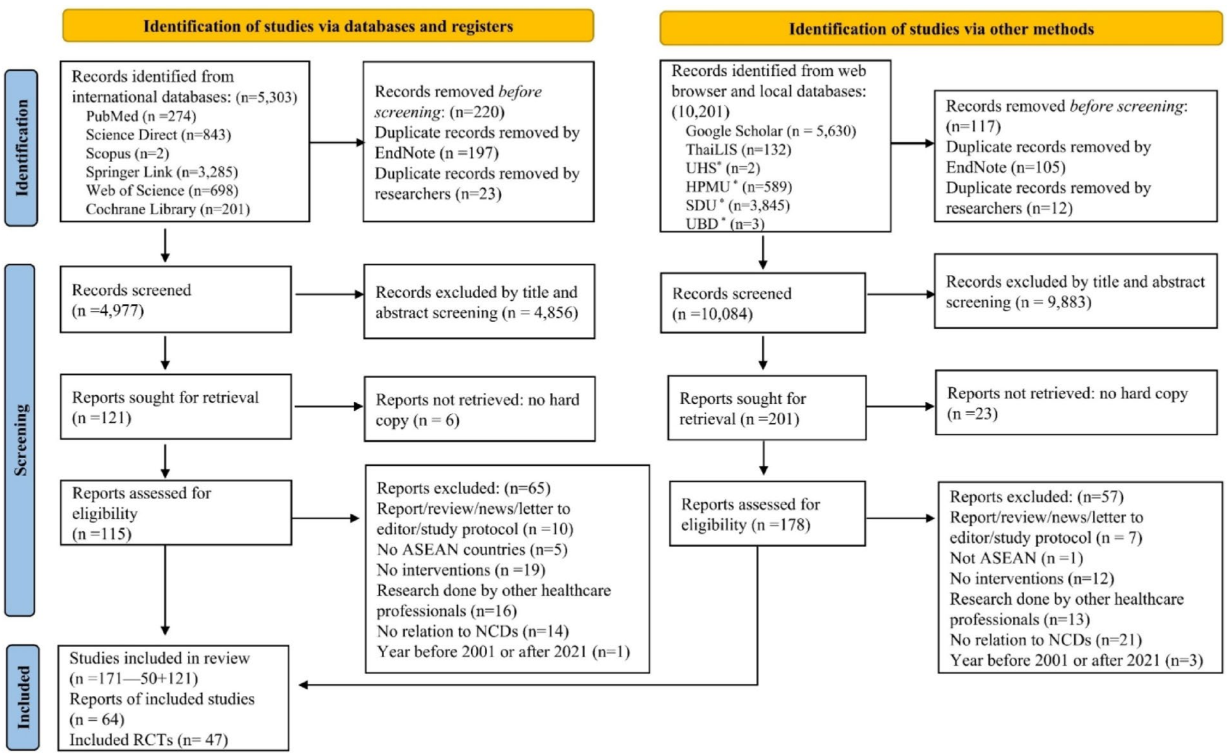

Fig. 1. PRISMA flowchart of study selection. *UHS* University of Health Sciences Lao, *HPMU* Haiphong University of Medicines and Pharmacy, *SDU* Sanata Dharma University, *UBD* University Brunei Darussalam.

(21.6%) and smoking cessation (9.4%). In terms of NCD clinical conditions, studies were conducted in kidney disease (2.3%) and heart failure (2.3%) (Supplementary Table S5). Of 171 included studies, 107 (62.6%) were published articles, while 64 (37.4%) were unpublished such as theses or research reports (Supplementary Table S5).

For the 47 RCT studies, the characteristics are presented in Supplementary Table S6. The study sites covered four countries: Thailand, Malaysia, Lao PDR, and Indonesia. Pharmacists' interventions varied from one to 12 months. Most of the studies were performed in hospital settings, with only six conducted in community pharmacies, primary care units, or schools. Of 47 RCT studies, 22 (46.8%) were published in journals, the remaining 25 (53.2%) were theses and reports.

Study quality assessment

Quality assessment of 171 studies using the MMAT and CASP is summarized in Supplementary Table S7. The risk of bias in the 47 RCTs is summarized in (Fig. 2a,b). From five domains of assessment: (1) seven studies were rated low risk for selection bias or randomization process, (2) six studies were rated low risk for performance bias or deviations from intended interventions, (3) 31studies were rated low risk for attrition bias or missing outcome data, (4) 13 studies were rated low risk for detection bias or measurement of the outcome, and (5) 34 studies were rated low risk for reporting bias or selection of the reported result. Nevertheless, considering all five domains collectively, only one study was judged to have an overall low risk of bias (Fig. 2b).

Pharmacy education outcomes

Classroom-based interventions related to NCDs and NCDs-related risk factors in pharmacy education were identified in seven studies. The topics included asthma, COPD, diabetes, hypertension, cardiovascular diseases, and smoking. Interventions were practice in providing pharmaceutical care, screening people who were at risk for diabetes and hypertension, teaching courses, and online training courses. Most of the results showed improvements in skills (inhaler use) and knowledge (screening, tobacco, and cardiovascular diseases).

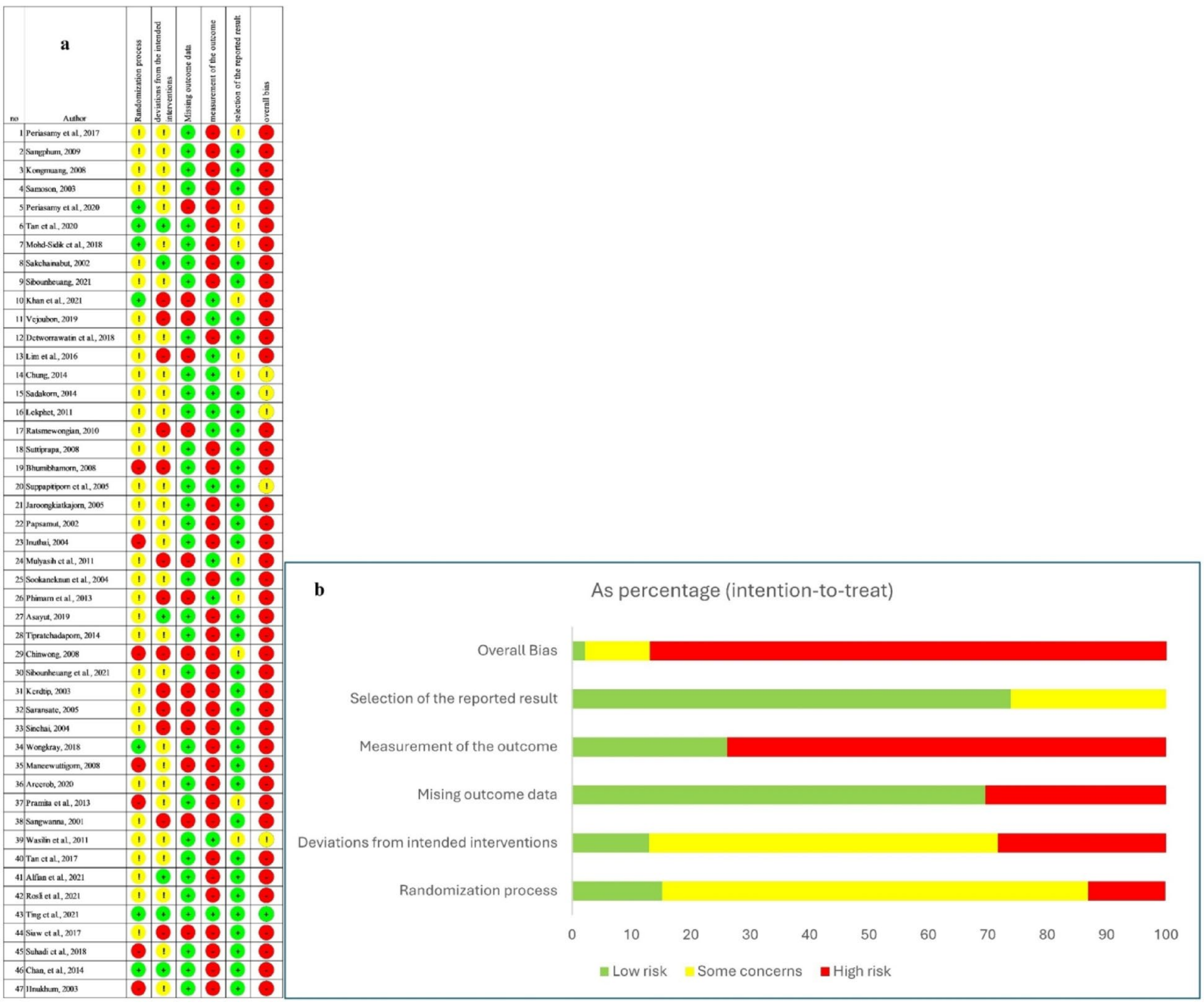

Fig. 2. Risk of bias in individual studies.

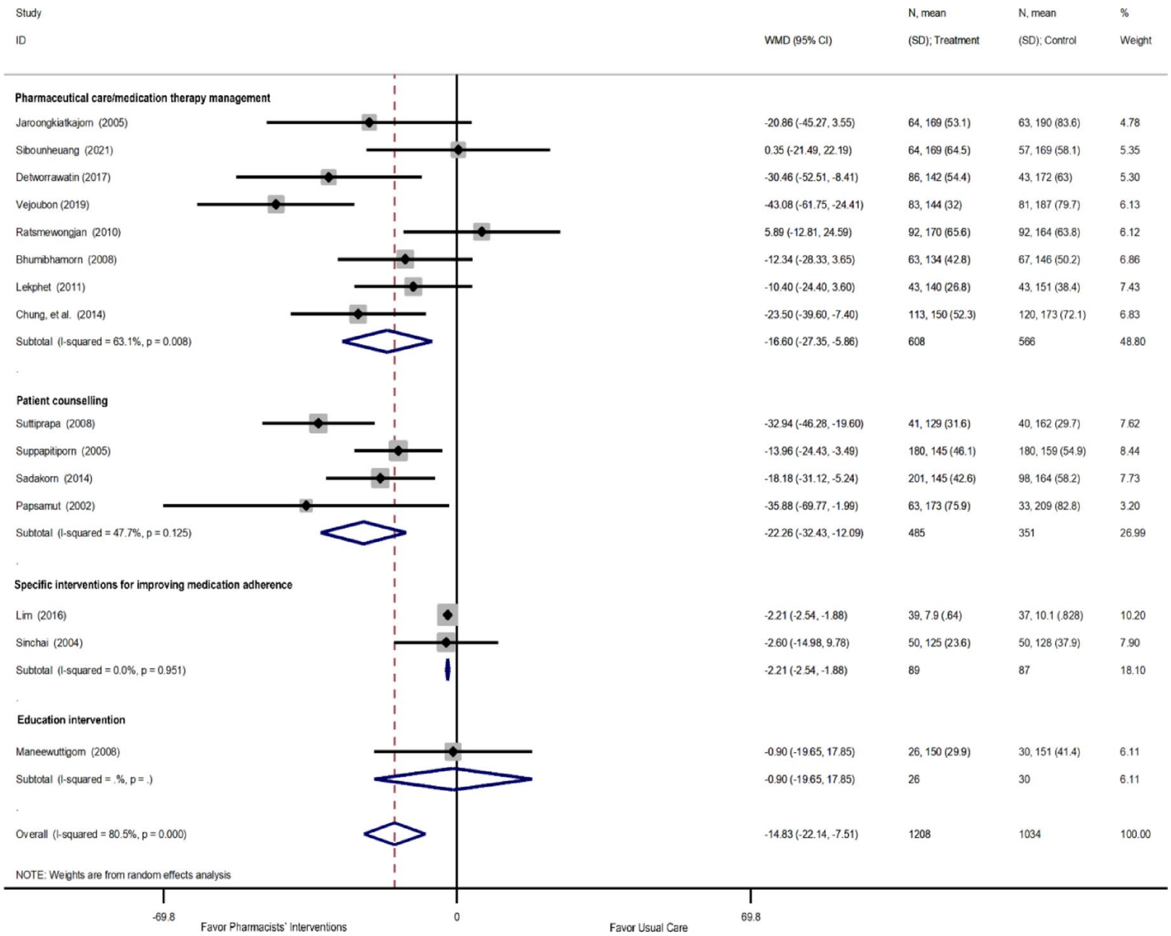

Fig. 3. Forest plot: effect of pharmacists' interventions on FBG level.

Nevertheless, one study showed no significant change in students' perceptions of physician-pharmacist interprofessional clinical education (Supplementary Table S4).

Pharmacy practice outcomes

Pharmacists' interventions were of four types: (1) patient counselling, including group and individual counselling, telephone follow-up, counselling sessions, counselling with booklets and medication containers; (2) pharmaceutical care relating to medication therapy management at clinics and homes, at homes, with Subjective, Object, Assessment, and Plan (SOAP) notes, using low glycemic rice, and mobile application; (3) specific intervention on medication adherence including pharmacist-initiated medication refills, and interventions to improve medication adherence; and (4) education (Supplementary Table S4).

Effect of pharmacists' interventions on diabetes outcomes

Pharmacists' interventions in diabetes were reported in 59 studies. Of these studies, 43 studies reported clinical outcomes; one report showed contradictory outcomes between HbA1c and FBG[30]. The results showed more positive (28 studies) than negative (15 studies) outcomes after pharmacists' involvements (Supplementary Table S4).

Thirteen RCT studies[30–42] involving 2,242 patients were included in the meta-analysis assessing impact of pharmacists' interventions on FBG levels. Pooled estimates demonstrated a statistically significant reduction in FBG level compared to usual care (WMD – 14.83, 95% CI -22.14 to -7.51, I^2 80.5%). The effects were statistically significant when pharmacists delivered pharmaceutical care, patient counselling, and specific interventions for improving medication adherence (Fig. 3).

Seventeen RCT studies[30–41,43–47] measuring HbA1c in 2,600 patients were included in the meta-analysis. Pooled estimates showed a statistically significant reduction in HbA1c compared to usual care (WMD – 0.60, 95% CI -0.75 to -0.45, I^2 50.8%). The effects were statistically significant when pharmacists provided pharmaceutical care, patient counselling, and specific interventions for improving medication adherence (Supplementary Fig S3).

Nine RCT studies involving 1,285 patients reporting FBG control (≤ 130 mg% [30,32–34,36–39], one study used ≤ 140 mg% [48]) were included in the meta-analysis. Pooled estimates demonstrated that interventions resulted in a statistically significant improvement of FBG goal achievement (RR 1.47, 95%CI 1.03–2.09, I^2 71.6%), however the heterogeneity was substantial (Supplementary Fig S4).

Nine RCT studies [31–34,36–39,41] involving 1,302 patients that reported HbA1c control (< 7%) were included in the meta-analysis. Pooled estimates demonstrated no significant difference in achievement of HbA1c goal compared to usual care. A statistically significant improvement was found in one study when pharmacists delivered patient counselling (Supplementary Fig S5).

Most studies demonstrated that pharmacists' interventions improved medication adherence, quality of life, and satisfaction, although a few studies reported no significant differences. Three qualitative studies highlighted the need for a plan to promote rational drug use in diabetes patients in Thailand, while a pharmacist-managed diabetes clinic in Singapore fulfilled patients' needs for health information. Nevertheless, one qualitative study from Indonesia reported that community pharmacists provided insufficient information (Supplemental Materials: page 26–28).

Effect of pharmacists' interventions on smoking cessation outcomes

Pharmacists' interventions in smoking cessation were reported in 16 studies. Of these, 13 studies focused on interventions for smokers, especially counselling (including an application or medications), and education, and three studies focused on training pharmacists to perform smoking cessation services. Of 10 studies assessing clinical outcomes (e.g., quite rate, %PEFR) seven studies showed positive and three studies showed negative outcomes after pharmacists' involvement (Supplementary Table S4). The peak expiratory flow rate (or %PEFR) is an objective measure of airflow limitation; the normal range is at least 80%[49].

Three RCT studies[50–52] involving 319 smokers were included in the meta-analysis. Pooled estimates demonstrated no significant changes in quit rates when compared with usual care (Supplementary Fig S6).

In addition, pharmacists' interventions improved patient knowledge, quality of life, and awareness of need to quit smoking after counselling. Pharmacists who received training applied their skills in practice; however, follow-up arrangements were infrequently implemented. Cost savings from pharmacists' interventions were reported at $515 (17,503 baht) for men and $632 (21,499 baht) for women. life years gained were 0.18 (men) and 0.24 (women)[53].

Effect of pharmacists' interventions on asthma and COPD outcomes

Pharmacists' interventions were reported in 11 studies in asthma and four studies in COPD. Of these studies, eight asthma studies reported clinical outcomes such as forced expiratory volume in one second (FEV1), PEFR, %PEFR, or asthma control. One COPD study reported PEFR.

Overall, more positive outcomes (six studies) than negative (three studies) outcomes were observed after pharmacists' interventions (Supplementary Table S4).

Four RCT studies[50,54–56] were undertaken in 291 asthmatic patients; three studies[50,54,55] reported %PEFR and four studies[50,54–56,57] reported PEFR were included in the meta-analysis. Pooled estimates demonstrated statistically significant improvement of %PEFR and PEFR with pharmacists' interventions compared to usual care (WMD 9.11, 95% CI 1.09 to 17.13, I^2 59.8%) (Supplementary Fig S7).

Four RCT studies[50,54,56,58] involving 347 patients reporting asthma control were included in the meta-analysis. Pooled estimates showed no statistically significant difference in asthma control compared with usual care (Supplementary Fig S8).

A single COPD study showed significant PEFR improvement in patients who received pharmacists' interventions compared to usual care ($p < 0.05$)[57].

Other outcomes, such as drug related problems, satisfaction, knowledge, adherence, and quality of life, were reported positively, although a few studies found no significant differences. Cost of pharmaceutical care services was reported to be $10.50 (356 baht) per person[58].

Effect of pharmacists' interventions on hypertension outcomes

Pharmacists' interventions were reported in 37 studies in hypertension management and three studies focused on screening and education for people at risk. Twenty-nine studies reported blood pressure outcomes which showed both positive (17 studies) and negative (14 studies) clinical outcomes observed after pharmacists' involvement (Supplementary Table S4).

Fifteen RCT studies[18,30,33,34,36–40,45,59–63] that reported systolic blood pressure (SBP) and diastolic blood pressure (DBP) involving 2,015 patients were included in meta-analysis. Pooled estimates of 15 studies demonstrated statistically significant differences in reducing SBP (WMD – 2.60, 95% CI -5.10 to -0.11, I^2 81.9%) and DBP (WMD – 1.31, 95% CI -2.22 to -0.40, I^2 42.3%) when compared with usual care (Supplementary Fig S9-S10).

In subgroup analysis, the pooled estimates of four studies focusing specifically on hypertension[18,59,60,63] showed that pharmacists' interventions were effective in lowering SBP compared to usual care. However, there was no statistically significant difference between groups for the 11 diabetes studies that also assessed blood pressure[30,33,34,36–40,45,61,62] (Supplementary Fig S11).

Blood pressure control was reported from six RCT studies with 711 patients[18,30,33,36,59,64]. Pooled estimates of six studies demonstrated no statistically significant differences (Supplementary Fig S12).

In addition, pharmacists' interventions for screening showed positive outcomes in diet behaviour but not exercise and body mass index (BMI). Most studies which reported humanistic outcomes showed that pharmacists' interventions positively impacted adherence, quality of life, lifestyle modification, knowledge, and satisfaction, but a few studies did not show significant differences. Unit cost of screening services was reported $11.20. (Supplementary Materials: page 26–28).

Effect of pharmacists' interventions on lipid outcomes

Pharmacists' interventions were reported in two studies focused on dyslipidemia. Only one study reported positive clinical outcomes (Supplementary Table S4). However, studies targeting other conditions also reported lipid outcomes which were included in the meta-analysis.

Five studies[30,33,34,38,39] of total cholesterol (TC) that involved 765 patients, and six studies[30,33,34,34,38,39] of triglycerides (TG), low-density lipoprotein cholesterol (LDL-C) and high-density lipoprotein cholesterol (HDL-C) that involved 929 patients, were included in the meta-analyses. Pooled estimates of the five studies on TC and six studies on TG, LDL-C, and HDL-C, demonstrated pharmacists' interventions statistically significantly improved TC, TG, LDL-C and HDL-C levels when compared to usual care (TC, WMD − 7.42, 95%CI -13.59 to -1.26, $I^2 = 0.0\%$; TG, WMD − 20.19, 95%CI -39.28 to -1.11, I^2 57.0%; LDL-C, WMD − 4.96, 95%CI -9.78 to -0.13, I^2 0.0%; HDL-C, WMD 2.49, 95%CI 0.12 to 4.86, I^2 52.2%).

The effects on TC, TG, and HDL-C were statistically significant when pharmacists delivered pharmaceutical care. Meanwhile, for patient counseling from one study[39], a statistically significant difference in LDL-C was found (Supplementary Fig S13-S16).

Effect of pharmacists' interventions on other outcomes

Pharmacists' interventions in cardiovascular diseases, stroke, and warfarin use were reported in 13 studies which were mainly conducted in one-group and quasi-experimental designs. These interventions showed positive outcomes in terms of hospital admissions for heart failure, lipid profile, and blood pressure (Supplementary Table S4). Of the two studies involving warfarin use, only one RCT study reported clinical outcomes demonstrating a significant benefit of pharmacists' interventions, with the time in the therapeutic range being higher in the intervention group compared to the control group ($p = 0.046$)[65].

Of the two studies that involved obesity, only one study (RCT) reported clinical outcomes. The pharmacist's intervention on weight reduction at weeks 0, 4, 8, and 16 did not show significant improvement when compared with the control group.

Of 13 studies in cancer patients, only one study (RCT) reported clinical outcome. The pharmacists' interventions showed an achievement of major molecular response at month 6[66]. In addition, pharmacists' interventions positively impacted patients' knowledge, self-care, satisfaction, quality of life, self-esteem, depression and anxiety, and medication adherence. However, one study did not show significant differences in quality of life compared to usual care. The cost of providing counselling and education to parents of children with cancer was estimated at 35, 14, and 11 baht for visits 1, 2, and 3 over a 4-month period (Supplementary Materials: page 26–28).

Subgroup analysis, sensitivity analysis and publication bias or small study bias test

Subgroup analyses based on types of pharmacists' intervention were conducted for most outcomes (Fig. 3, Fig S3-S7, S9-S16). Visual inspection of the funnel plot and the Egger regression test found evidence of small-study effects for FBG levels (Supplementary Fig S17A-P). Subgroup analyses of the significant pooled estimates from the main analysis demonstrated varying results in the subgroups. For example, while the pooled estimate for achieving FBG goals were significantly different between the intervention and control groups, neither pharmaceutical care nor pharmacy counseling showed significant differences when compared with usual care (Fig S4).

Pre-specified sensitivity analyses restricted to trials without high risk of bias were not performed because most of the included studies were assessed to have a high risk of bias. Two additional sensitivity analyses, not outlined in the protocol, were conducted. First, a sensitivity analysis excluding small-sample-size studies (fewer than 30 participants per group)[67] was performed for FBG and HbA1c outcomes, based on the available data. The results for for both FBG and HbA1c were consistent with those of the main analysis (Supplementary Fig S18-S19). Second, sensitivity analysis excluding theses was conducted based on the existing data (Supplementary Fig S20-S24), only the FBG outcome differed from the main analysis, showing no significant differences between pharmacists' interventions and usual care, along with considerable heterogeneity (WMD − 16.65, 95%CI -36.19 to 2.90, $I^2 = 84.6\%$) (Fig S20).

Discussion

From the 10 ASEAN countries, 163 studies related to pharmacy education and practice in NCDs were identified from seven countries. Of these studies, 39% were theses and reports. Aiming to explore pharmacy practice for primary prevention and management of NCDs, this review found that pharmacists' interventions addressed major NCDs, six risk factors, and two clinical conditions. Pharmacy education demonstrated positive outcomes in students' skills and knowledge related to NCDs, particularly asthma, diabetes, hypertension and tobacco use. Pharmacists' interventions were associated with positive clinical outcomes identified through meta-analyses, including reductions in FBG, HbA1c, TC, TG, and HDL-C, as well as in SBP among hypertensive patients. Improvements in %PEFR were also observed among asthma patients. Furthermore, the improvements in achieving FBG, and HbA1c goals were seen in the counselling intervention subgroup. Nevertheless, significant heterogeneity was found in studies for FBG levels and achievement of HbA1c goals. Other positive clinical outcomes included reduced hospital admissions for heart failure, improved time in the therapeutic range for warfarin use, and achievement of major molecular response in cancer treatment. Nevertheless, no significant weight reduction was observed in patients with obesity. Overall, pharmacists' intervention tended to improve adherence, satisfaction, knowledge, and quality of life.

To our knowledge, this is the first systematic review and meta-analysis of studies assessing the impact of pharmacist intervention in NCDs in the ASEAN region. We included a high number of studies and accounted for multiple components of the interventions to explore the effect of possible bias. To characterize the impact of pharmacists in the ASEAN region, the randomized controlled trials used included published and unpublished studies to reduce the risk of publication bias.

For classroom-based interventions, two studies were undertaken in the areas of tobacco use and smoking cessation; and two intervention studies were carried out to assess screenings, which play a vital role in the early detection and management of NCDs, potentially reducing NCD risks and improving patients' outcomes. These interventions align with the goal of reducing mortality from NCDs as emphasized by SDG target 3.4[10] and the WHO Framework Convention on Tobacco Control (FCTC) on effective education (Article 12) and smoking cessation (Article 14)[68]. Nevertheless, studies in pharmacy education aimed at preparing students to care for NCDs patients or people who have NCD-related risk factors were still limited, particularly in terms of practice, knowledge, and attitude outcomes. Given the diverse curricula, limited faculty, and constrained scope of NCD teaching[24] in the ASEAN countries, there is a need for stronger support and further research in pharmacy education to better serve pharmacy practice.

This study found significant positive outcomes for pharmacists' interventions in continuous outcomes for various conditions including diabetes, asthma, hypertension, and lipid disorders. However, there were considerable heterogeneities in studies of FBG and achievement of HbA1c goals. One possible explanation for this could be that the study timeframes varied from one month to 12 months for FBG and HbA1c, and the timeframes for asthma were five to six months. Another explanation could be variations in pharmacists' interventions. For example, one study compared a pharmacist-led refill clinic for diabetes to a physician-led clinic; the results showed no differences between groups[41]. Thus, subgroup analysis by four types of pharmacists' interventions (pharmaceutical care, patient counseling, specific interventions for improving medication adherence, and education) were performed and showed that patients who received all pharmacists' interventions except education, significantly reduced both FBG, and HbA1c levels. Interestingly, the patient counseling subgroup showed significantly better achievement of HbA1c goals, while other subgroups did not. Nevertheless, the heterogeneity in subgroup analysis in FBG was still substantial (I^2 = 47.7% for pharmacy counseling; 63.1% for pharmaceutical care and medication therapy management). Two studies that did not show significant differences between groups were conducted in Lao PDR[33] and Thailand[37]. Although both studies focused on individual care plans including SOAP notes[37], they reported a lack of therapy modification for diabetes based on FBG during the study period[33,37], as well as time constraint[33].

In addition, there were significant differences in both systolic and diastolic blood pressure from 15 studies, but subgroup analyses found that the subgroup with only hypertension had a significant SBP reduction with pharmacists' interventions compared to usual care. While studies of pharmacists' interventions using medication therapy management elsewhere[14–16] have improved patient outcomes[69], pharmacists' interventions in ASEAN countries did not show positive clinical outcomes for the achievement of all treatment goals. Enhancement of the pharmacists' skills as healthcare team members should be supported to enable pharmacists to help patients achieve their clinical goals.

The humanistic outcomes such as adherence, knowledge, satisfaction and quality of life showed positive responses to pharmacists' interventions. The studies covered a range of conditions including asthma, obesity, cancer, diabetes, hypertension, smoking cessation, and warfarin use, and utilized various questionnaires. Evidence of strong physician acceptance of pharmacists' care and excellent patient satisfaction has supported the development and advancement of pharmacists' roles in the U.S.A., supported by research and changes in state laws governing pharmacy[20]. Further research can strengthen the evidence regarding pharmacists' contributions to quality of care, especially in prevention and management NCDs and associated risk factors, and could serve as a key mechanism for advancing pharmacy practice and improving health outcomes across the ASEAN region.

This study has several limitations. First, several RCT studies lacked sufficient information, particularly regarding the randomization process, reasons for subject dropout, blinding methods, and lack of a pre-published protocol. Consequently, most studies were at high risk of overall bias and our findings should be interpreted with caution[64]. One may assume that each randomized study was conducted properly but not reported in detail, but this cannot be verified. In clinical practice research, blinding is often difficult to implement, especially for accessors, therefore, quality assessment should consider other information such as baseline characteristics and types of outcomes. Since the individual studies were randomized and reported objective clinical outcomes, lack of blinding should not greatly impact results. Second, the study protocol did not exclude small studies. However, sensitivity analysis that excluded small studies (n < 30 participants) was performed and the results were unchanged. Third, due to concerns about methodological rigor of theses, during the review process an additional sensitivity analysis was performed by excluding them. Only the result for FBG levels differed from the main analysis, showing no significance between groups with consistently considerable heterogeneity (I^2 = 84.6%). However, when analyzing theses alone for FBG levels, the result aligned with the main analysis, showing a significant difference between groups with a substantial heterogeneity (I^2 = 64.2%). Thus, the inclusion of theses increased the power of the meta-analysis for positive FBG results. Moreover, the inclusion of unpublished theses and reports adds value by minimizing publication bias. Fourth, two out of seven local databases could not be included as originally planned because of limited access. Fifth, this study used four medical/biomedical databases: PubMed, Scopus, Web of Science and CINAHL. However, during the study, access to CINAHL was discontinued, and it was replaced with Springer Link. Since CINAHL focuses on nursing literature, its exclusion is not expected to significantly impact the study's findings. While Google Scholar search strategies identified over 1,000 results, we decided not to screen these studies because of limitations of time and labor. Lastly, the RCT studies were conducted in only four of the ten ASEAN countries, so the results may not be fully generalizable.

As 37.4% of the studies included were theses by master's and PhD students, these studies demonstrated the contributions of academic researchers. Universities, as centers of research and knowledge creation[70], should encourage students to participate in practice research projects to enhance students' understanding of real-world challenges and this would also contribute to the evidence base for preventing and treating NCDs. A strong academic process for graduate theses typically involves multiple examinations, often including external professional examiners. However, some theses or reports may remain unpublished for various reasons, such as the absence of a publication requirement for graduation, time constraints, or small sample sizes. By including these unpublished theses and reports, this study adds value by minimizing publication bias and ensures a more comprehensive evidence base. Furthermore, combining small-sample studies from local countries through meta-analysis enhances the statistical power to detect meaningful differences in intervention effects. Further suggestions include additional efforts to increase publications in peer-review journals, conducting collaborative studies with pharmacists to strengthen evidence, and initiating larger, long-term studies. Additionally, with over 500 schools of pharmacy across the 10 ASEAN countries[71], a network from these schools could support, exchange, and guide research, pharmacy training, programs, and innovations (e.g. medical technologies)[72] aimed at advancing pharmacy practice and education for the prevention and management of NCDs in the region.

Conclusion

Our comprehensive review highlights the limit of pharmacy education in ASEAN countries regarding provision of care for patients with NCDs. Pharmacist-led interventions have demonstrated benefits for NCD patients, especially in providing care for diabetes, hypertension, lipid disorders, and asthma. These interventions also led to positive humanistic outcomes. Nevertheless, due to a high overall risk of bias, the results should be interpreted with considerable caution. Larger, more comprehensive, long-term, and methodologically rigorous studies are needed to further assess and support the contributions of pharmacists in the ASEAN region.

Data availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Received: 30 December 2024; Accepted: 15 October 2025
Published online: 20 November 2025

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Acknowledgements
The authors would like to thank Mahasarakham University in Thailand for financial support, and Academic Resource Center at Mahasarakham University for support with literature searching for full texts. Thank you so much to Lien Ngo for translating some studies in Vietnamese to English and also assessing MMAT for some studies.

Author contributions
All authors contributed to the study conception and design. Material preparation and data collection were performed by Bee Kim Tan, Theerapong Seesin, Christianus Heru Setiawan, Suntree Watcharadamrongkun, Nguyen Van Hung, Phoutsathaphone Sibounheuang, Nurolaini Kifli, Juntip Kanjanasilp, Santiparp Sookaneknun, Thi La Do, Chanuttha Ploylearmsang, and Phayom Sookaneknun Olson. The first draft of the manuscript was written by Phayom Sookaneknun Olson, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Funding
This research project was financially supported by Mahasarakham University, Thailand [6502008]. Olson PS has received research support from Mahasarakham University.

Declarations

Competing interests
The authors declare no competing interests.

Additional information
Supplementary Information The online version contains supplementary material available at https://doi.org/10.1038/s41598-025-24749-3.

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