

PHARMACISTS INTERVENTION REDUCED DRUG-RELATED PROBLEMS IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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Abstract.

estimated 463 million (9.3%) of the world's population in adults aged 20-79 years suffering from diabetes. Without sufficient action, it was estimated that 578 million people (10.2% of the population) will have diabetes by 2030. Indonesia ranked 7th country in the world with the number of diabetics (10.7 million), estimated to increase to 13.7 million in 2030. Effective diabetes management often presented big challenges. One of the things that can prevent or delay patients from achieving the goals of T2DM therapy was related to drug therapy or known as drug-related problems (DRP's). Pharmacist clinical intervention can have a positive impact on patient treatment. Pharmacist intervention was always considered valuable involvement by the health care community in the process of patient treatment in reducing medication error, rationalizing therapy and reducing therapy cost. Objectives: This study aimed to identify and review original articles in evaluating pharmacist intervention in the management of diabetes mellitus on drug-related problems (DRP). Methods: Review the PubMed and ProQuest database to identify management evaluation of T2DM therapy. The inclusion criteria used in this study were all original research articles published between 1999 until 2017 regarding pharmacist interventions on DRP. Articles were assessed using the Prisma checklist. Results: 4 articles related to this study. Patients with T2DM were at risk of experiencing drug-related problems (DRP), which can occur at every step during the treatment process and affect the result of therapy. The average DRP value were quite high at 4.1 to 4.6 DRP per patient. Conclusions: Pharmacist interventions helped increase the quality of treatment and reduced health care costs. Patient education and counseling from pharmacists to identify and resolve drug-related problems (DRP) and improve treatment compliance can help achieve the goals of managing diabetes mellitus therapy.

Keywords: Pharmacist interventions, drug-related problems (DRP), diabetes mellitus therapy

1. INTRODUCTION

Presently, diabetes is a major health problem which has reached alarming levels. Nearly half a billion people live with diabetes worldwide (1). Globally, there were estimated 463 million (9.3%) of the world's population in adult aged 20-79 years suffering from diabetes (1). Without sufficient action, it was estimated that 578 million people (10.2% of the population) will have diabetes in 2030. Indonesia ranked 7th country in the world with the number of diabetics

(10.7 million), estimated to increase to 13.7 million in 2030. This figure will surge to 700 million (10.9%) in 2045 (1). More than 60% of diabetics were in the Asian region (1,2). China was the Asian country with the highest prevalence of diabetes (116.4 million) in 2019 (1). Indonesia ranked 7th country in the world with the number of diabetics (10.7 million), estimated to increase to 13.7 million in 2030 and will continue to increase to 16.6 million in 2045 (1). The increasing prevalence of diabetes could be attributed to many factors such as rapid industrialization, urbanization and lifestyle changes (3).

International Diabetes Federation divided diabetes into two categories, namely type 1, type 2, gestational and other types of diabetes (1). Type 2 diabetes mellitus (DMT 2) contributes 90-95% of the incidence of diabetes and was related to genetic factors, age, obesity and lack of physical activity (1,4).

T2DM caused dysfunction in many organs and tissues. Chronic hyperglycemia in T2DM was also associated with long-term damage, and failure of different organs, especially the eyes, kidneys, nerves, heart, and blood vessels which results in increased levels of morbidity and mortality (5,6).

Effective diabetes management often presented big challenges. One of the things that prevented or delayed patients from achieving the goals of T2DM therapy was related to drug therapy or known as drug-related problems (DRP's) (4). According to the Pharmaceutical Care Network, drug-related problems were defined as events or circumstances involving drug therapy that actually or potentially interfere with the desired health results (11,12). DRP's could be in the form of polypharmacy (use of ≥ 5 drugs), improper drug selection, improper dosage selection, adverse drug reactions, drug interactions, contraindications, and non-compliance (7-10).

Pharmacist clinical intervention had a positive impact on patient care. Interventions by pharmacists were always considered valuable input by the health care community in the process of patient care by reducing medication errors, rationalizing therapy and reducing therapy costs (11).

In managing DMT2 patients, partnerships between various diabetes experts including pharmacists, nurses, and nutritionists had been proven to provide comprehensive care that meets the needs of patients. In collaborative management of diabetic patients, pharmacists, nurses, and nutritionists were able to optimize medicines, provided motivational counseling on self-care practices and gave advice on nutritional therapy (11,12).

II. METHODS

Examination Strategy

Studies on pharmacist interventions in the management of type 2 diabetes mellitus were sought in ProQuest, and PubMed/MEDLINE uses the keywords "interventions (pharmaceutical care, evidence base pharmacy practice), drug-

related problems, type 2 diabetes mellitus".Data sources were obtained online, then selected based on inclusion and exclusion criteria. Inclusion criteria are all sources, full text, and main articles in English. The systematic search for articles was carried out using PubMed/MEDLINE and Pro Quest. The term used for searching this review are combination of "Diabetes Mellitus, Type 2" OR "Diabetes Mellitus," OR "Type 2 Diabetes Mellitus" OR "Type 2 Diabet * [tw]" AND "Pharmaceutical services" OR "Services, Pharmaceutic "OR" Pharmac* intervent*tw] "AND" Medication error "OR" Polypharmacy "OR" Drug Related Side Effects "OR" Adverse Reactions "OR" Drug related Side "OR" Drug Related Side "OR" Effects and Adverse Reactions "OR "Drug interactions" OR "Drug Misuse, Prescription" OR "Drug Contraindications" OR "Multidrug Resistance" OR "Patient Medication Knowledge".

Inclusion Criteria

Article in English about pharmacist interventions were related to drug-related problems in the treatment of type 2 diabetes mellitus. The process of selecting or screening articles to conclude full articles were needed (free full article), in humans, journal articles, in English, MeSH Term and published in some countries without year restrictions.

Information from the extraction process

Information needed to obtain intervention analysis of drug-related problems were from the article using Prisma checklist guide. The criteria needed for each article were listed in table 1.

Table 1. Pharmacist intervention criteria of drug-related problems in the treatment of type 2 diabetes mellitus

Research design	setting dan location
	tiipe of study
	study perspective
	time horizon
Information about diabetes melitus	General informationabout type 2diabetes mellitus
	Strategicmanagement of diabetes mellitus treatment
	Study of diabetes mellitus effectiveness
	Drug-related problems
Outcome measurment	Choice of health outcome
	Cost effectiveness criteria
Result	Pharmacist intervention
	Compliance to patientof tiipe 2diabetes mellitus

III. RESULT AND DISCUSSION

The purpose of systematic review was to find out the results of pharmacist intervention research on DRP in the management of type 2 diabetes mellitus in all countries. The articles obtained that were suitable for the inclusion criteria from the PubMed/MEDLINE database were 127 articles and from Pro Quest were 20 articles. We selected 6 articles after excluding 123 articles from PubMed and 20 articles from ProQuest, because they were pharmacological and epidemiological studies. From these 6 articles, we selected 4 articles that were suitable for the final review, as presented according to the chart below.

Our 4 selected studies come from 4 different countries: The longest article that appeared in our search came from 1999, focusing on pharmacist interventions on T2DM drug-related problems in all countries namely: New South Wales Australia, Denmark, Norway and Singapore.

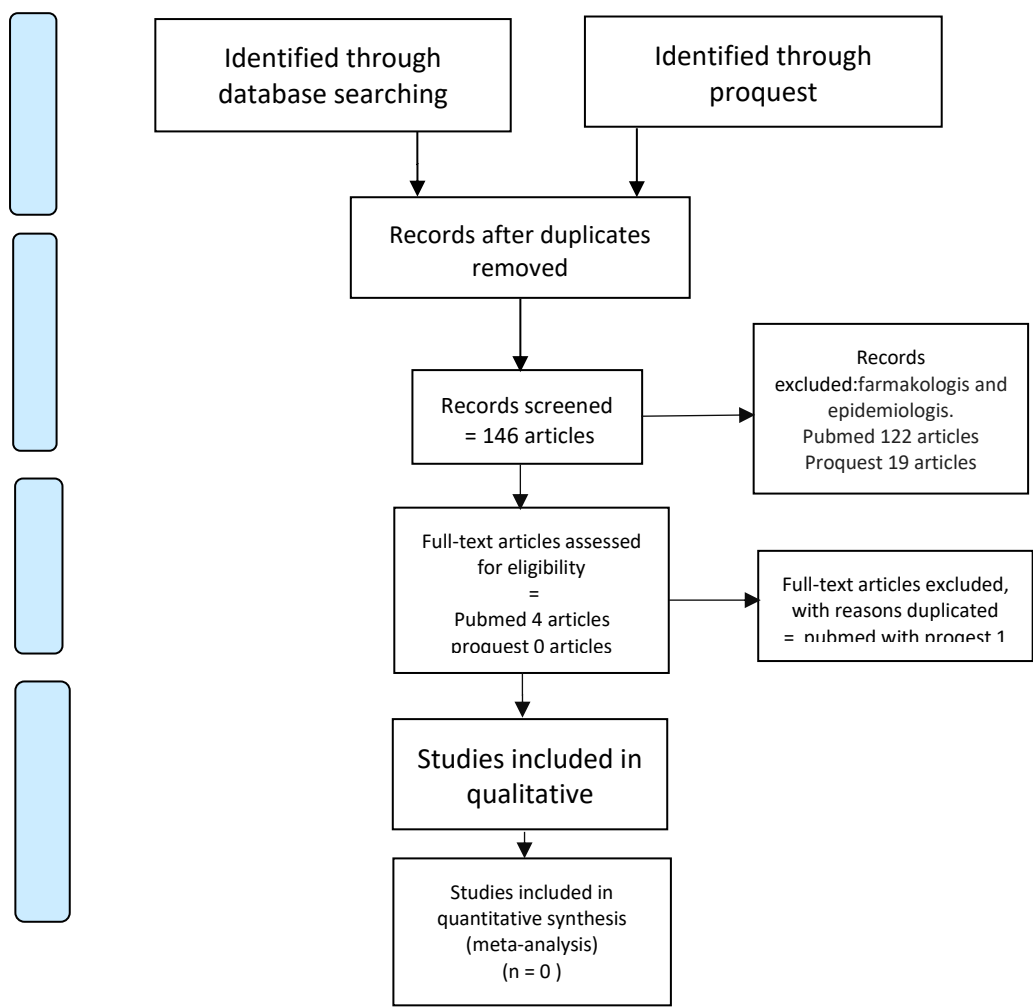


Fig. 1. Prisma Flow Diagram

Based on article screening, there were obtained four articles that suitable for criteria and are relevant to pharmacist intervention in reducing DRP in the treatment of type 2 diabetes mellitus. The articles were reviewed using the Prisma checklist covering the method (study design) and the results of the study. The results of the review based on the method used from the four articles can be seen in Table 2 and Table 3.

Table 2.

Study	Title	Target population and subgroups	Setting location and Time	Abstract (structured summary)	Introduction (Rationale, Objectives)
Roozend aal, B.W., Krass I.E., 2009	Development of an evidence-based checklist for the detection of drug-related problems in type 2 diabetes	Outpatients with Type 2 Diabetes	New South Wales Australia, 2009	- <i>Background</i> :Develop Checklist based on Potential Drug Related Problem (PDRP) - <i>Method</i>: The first step was a comprehensive review of the literature by identifying patients with drugs that are relevant to the problem of DRP - <i>Result</i>: The checklist can help pharmacists and health care professionals	<i>Rationale :</i> - An evidence-based checklist can be used specifically in patients with type 2 diabetes, to help pharmacists and other health professionals systematically identify DRPs - There is a high prevalence of DRPs in a population of patients with type 2 diabetes and poor glycemic control. - DRPs in patients with type 2 diabetes in New South Wales have experienced failed therapy and problems in drug choice <i>Objectives :</i> - developing an evidence-based PDRP (potential drug-related problem) checklist that can be used to review patient status and drug

Study	Title	Target population and subgroups	Setting location and Time	Abstract (structured summary)	Introduction (Rationale, Objectives)
				to identify issues in the therapy and management of type 2 diabetes patients and allow previous interventions to improve metabolic control.	regimens to identify potential DRPs in type 2 diabetes.

Study	Title	Target population and subgroups	Setting location and Time	Abstract (structured summary)	Introduction (Rationale, Objectives)
Haugbolle, L.S., Sorensen E.	Drug-related problems in patients with angina pectoris, type 2 diabetes and asthma – inter-viewing patients at home	Pharmaceutical-based population of 414 patients who visited pharmacy, consisting of patients with angina pectoris, type 2 diabetes and asthma	Denmark 1999, 2000 and 2001	- Background: creating a basis for improving the quality of counseling practices in pharmacies - Methods: collecting data, conducting treatment reviews and home interviews, and identifying cases of DRP in 414 patients - Results: From the results of qualitative interviews with three groups of patients identified who experienced DRP in patients with angina pectoris of 2.8 DRP/patient, patients with type 2 diabetes mellitus 4.1 DRP/patient and in asthma patients 4.0 DRP/patient.	<i>Rationale</i> - documentation of DRP problems plays a role in the quality assurance of pharmaceutical care and the development of quality pharmaceutical practices - DRP documentation can be used to negotiate reimbursement of pharmaceutical services, health policies or as an indicator of the pharmaceutical practice process - A home interview between the pharmacist and the patient can be used to identify the DRP, because the patients feel more relaxed so that they can provide an overview and experience of treatment and illness, giving consideration, actions and problems. Patients can also display the contents of their medicine

Study	Title	Target population and subgroups	Setting location and Time	Abstract (structured summary)	Introduction (Rationale, Objectives)
					cabinet specifically
					<i>Objective</i> - Contribute to the quality of the development of pharmaceutical practices and pharmaceutical practice research in the area of pharmaceutical treatment.
Granas, A.G., et al., 2010	Evaluating categorisation and clinical relevance of drug-related problems in medication reviews	Patients with type 2 diabetes based on community pharmacy	23 farmasiko munitas di Norwegia	- Background: categorization and clinical evaluation can be used to identify relevant DRP by community pharmacists. Then, it was used to assess the quality of interventions in patients and doctors. - Method: structured treatment review	Rationale: - Pharmacists' reviews and interviews with patients can improve understanding of drug therapy to improve adherence and contribute to rational treatment

Study	Title	Target population and subgroups	Setting location and Time	Abstract (structured summary)	Introduction (Rationale, Objectives)
				based on the patient's treatment profile and patient interviews. An evaluation group of retro-spective group was evaluated. The clinical/practical relevance of each DRP and the quality of community pharmacist interventions with patients and physicians were scored. The average agreement between EG and community pharmacists was calculated using the modified version of the Fleiss Kappa coefficient - Results: Evaluation results showed the ability of community pharmacists to identify the high / medium clinical / practical relevance of DRP and to follow up DRP with patients and doctors well	- Many DRPs can be avoided by monitoring the effects of long-term treatment and identifying patients at risk - Pharmacists can improve adherence to diabetes treatment through providing patient education Objective: - Evaluate categorization and identify clinical practices relevant to DRP by community pharmacists - Test the quality of interventions in patients and doctors by pharmacists
Siaw, M.Y., et al, 20017	Impact of pharmacist involved collaborative care on the clinical, humanistic and cost	Patients in aged ≥ 21 years with uncontrolled type 2 diabetes, health and co-morbidity	Outpatient health facilities were located in Singapore , which included 3 ethnic Chinese, Malay and Indian	Background : - As the prevalence of diabetes increases, the doctor-centered approach model was challenged to be able to provide holistic care in Asia - A multidisciplinary collaborative care model can	Rationale: - The conventional model of care where doctors were the only caregiver to meet the needs of patients wasfound in Asia - Time constraints due to increased

Study	Title	Target population and subgroups	Setting location and Time	Abstract (structured summary)	Introduction (Rationale, Objectives)
	outcomes of high-risk patients with type2 diabetes (IMPACT): a RCT			effectively manage diabetes Method : - Randomized controlled trial in 4 outpatient health service institutions - The control group received care as usual with the direction of nurses and nutritionists. Whereas the intervention group (multi-disciplinary collaborative) was followed by directions from the pharmacist Results: - In the intervention group there was a decrease in HbA1c from 8.6% to 8.1% during 6 months of treatment, whereas in the control group it did not change - An increase in PAID and DTSQ, a reduction in the workload of doctors and an average cost of US \$ 91.01 for all patients in the intervention group	patient burden was a major obstacle for doctors to provide comprehensive care. So that doctors were only able to spend an average of 5 minutes per patient per visit. - In this population, treatment was often complicated by cultural beliefs, religious practices, polypharmacy, limited formularies and low adherence to self-monitoring of blood glucose (SMBG). - Evidence of its impact on quality of life and cost savings for this group of high-risk patients was not available. Objective: - The main goal was to compare the clinical impact of multidisciplinary collaborative care with physician-centered care in managing patients with diabetes.

Study	Title	Target population and subgroups	Setting location and Time	Abstract (structured summary)	Introduction (Rationale, Objectives)
					- The secondary objective was to evaluate the humanistic outcomes reported by patients, as well as the level of utilization and expenditure for diabetes-related health services between the two types of care approaches.

Table 3.

Study	Method	Result
Roozend aal, B.W., Krass I.E., 2009	- Ethical approval: - - Time horizon: 2004 - Method : • Development Checklist: - Literature review of pharmacotherapy of type 2 diabetes and risk management for its complications - Identification of drugs groups to be included in the tool - Identification of potential DRP associated with drug groups based on literature. - Organization of all relevant information in the form of a checklist - DRP categorization into the Pharmaceutical Care Network Europe (PCNE) classification category	- 682 DRPs were identified using the PDRP checklist - Adverse reactions: 29.1% of patients experience hypo-glycemia in the period of 1 month before registration - Drug Choice Problems: there were 206 times the DRP associated with drug choices with an average of 1.4 drug / patient choice problems • 60.8% did not receive antiplatelet therapy despite an increased risk of cardio vascular 48.0% did not receive lipid-lowering therapy • 13.5% did not receive antihypertensive therapy • 0.7% did not receive a blood glucose lowering prescription - Dosage problems: there were 40 times the dosage problems below the recommended range or an incorrect dosage regimen. 13 times were seen in the use of aspirin and ACE inhibitors. There were 27 times overutilization, 15 cases related to sulfonylurea followed by ACE inhibitors and metformin

Study	Method	Result
	- Use of the tool retrospectively in 148 patients with type 2 diabetes • PDRP checklist application - Cross-sectional retrospective of medical record data of patients with type 2 diabetes - Compliance was assessed using BMQ (Brief Medication Questionnaire) - The checklist instrument consists of six main parts: lifestyle management, glycemic control, blood pressure control, lipid control, platelet control and medication adherence • Data analysis - Clinical parameter analysis using independent-samples rank correlation spearman coefficient Student's t-tests to compare the average treatment of the two groups - Subject: - Expert: Pharmacists and other health care professionals - Participants: 148 patients with type 2 diabetes - Samples: drugs: antidiabetic (43.1%), antihypertensive (33.4%), lipid-lowering drugs (13.4%) and anti-platelet (10.2%).	- Drug use problems: related to non-compliance as a drug use interaction problem (17.6%) • 103 cases of potential interactions identified using the checklist • The most frequent potential for drug interactions is between ACE inhibitors and sulfonylurea or insulin. • 15 times were found, 'triple whammy' which is defined as the use of thiazide diuretics and ACE inhibitors or angiotensin II antagonists in combination with NSAIDs • Other common interactions include the use of low-dose aspirin and other NSAIDs, atorvastatin and simvastatin and macrolide antibiotics, sulfonylurea and antimalarial drugs and ACE inhibitors and angiotensin II antagonists. - Therapy failure: was the biggest DRP category (38.7%) of all problems. Treatment failure was assumed when blood glucose, blood pressure or lipid levels were not adequately controlled despite receiving drug therapy to treat metabolic disorders. The cause of DRP was unknown. An increase in blood sugar levels above the recommended value was found in 133 patients (89.9%), increased blood pressure was found in 69 patients (46.6%) and lipid levels failed to reach the expected value found in 62 patients (41.9%) – There was a real correlation between systolic blood pressure and the total number of DRPs reduced 'failure therapy' (Spearman's correlation $n = 0.19$; $P = 0.028$). - Potential non-adherent patients had significantly higher HbA1c compared to other patients (HbA1c 9.4 vs 8.5; 95% CI: -1.50 for -0.20).

Haugbolle, L.S., Sorensen E.W., 2006	- Ethical approval: - - Time horizon: 1999, 2000 and 2021 - Method : • Internship program: 4th year pharmacy students to get data on this study. ^ 0% of 288 pharmacies in Denmark provide an internship program • Patient group: First year (1999) the study was conducted on angina pectoris patients. The second year (2000) was conducted in patients with type 2 diabetes mellitus. And the third year (2001) was carried out in asthma patients. • Preparation: Internship students were educated and then trained to be able to conduct interviews • Interview : - Qualitative interviews were chosen as a method of collecting patient data to obtain in-depth knowledge about the drug from each patient and knowledge related to the disease - Interviews conducted using semi structured interviews - Interview framework: theories about the rules of drug use, ways to overcome disease and DRP. • DRP documentation - Documentation of DRP identification was based on PI doc (Problem Interview Documentation) coding form. Pi doc is a hierarchical system for documentation on intervention problems - The protocol was developed following three	- The most common DRP was found in three groups of patients in the A-E subcategory in the coding system and the F subcategory for other problems which include aspects of treatment - DRP in patients with angina pectoris • DRP found 329 cases of DRP in 118 patients with an average of 2.8 DRP per patient • Improper drug used by patients (72 cases) • Not enough knowledge about drugs (28 cases) • Consciously made the decision not to take their prescription drugs (23 patients). For example, patients did not take statins because they feel they have no effect or do not take anti-seizure drugs or take in smaller amounts because they cause headaches. • Incorrect dosage (52 cases) • Side effects (47 cases) • In other sub categories, 127 cases of DRP were found. 81 cases related to patient itself, inappropriate lifestyle choices (21 cases) and 30 cases of DRP with a physician's death. - DRP in type 2 Diabetes patients • Found 635 cases of DRP in 155 patients or equivalent to 4.1 DRP per patient • 171 cases related to improper drug use • 95 cases related to lack of drug monitoring • 57 cases related to improper drug selection. • Counter indications not considered in prescribing drugs (27 cases) • Side effects (55 cases) • In another problem subcategory, 296 cases of DRP were found, 268 cases were related to patients themselves. Example 130 cases related to improper lifestyle choices, 103 cases were found in patients with limited knowledge about their disease - DRP in asthma patients • 349 DRP cases were identified with 88 asthma patients, equivalent to 4.0 DRP per patient • 167 cases related to improper drug use. • Lack of treatment monitoring in 58 cases • Problems with the use of inhalators affected 52 patients. • Lack of knowledge about drugs found 18 cases
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sub-studies based on feedback from pharmacy students, pharmacists and researchers.

- The protocol included general information about DRPs, concise guidelines on when and what to do on DRP documents, and instructions on how to use the documentation form.

- This protocol also contained documentation forms with examples of clarifying when using different sub-groups.

- Subject:

- Expert: Pharmacists

- Participants: 414 patients consisted of 123 angina pectoris patients, 192 patients with type 2 diabetes, and 99 asthma patients. The selection of patients was done by the non-random sampling method.

- Exclusion criteria: patients with home care, patients with dementia, patients who cannot speak Danish and patients with psychotic disorders

- Inclusion criteria: - Patients with angina pectoris who are given fast relief or sustained release glyceril nitrate

- Patients with type 2 diabetes who get oral antidiabetic or insulin.

- Asthma patients who get every type of asthma medication

Study	Method	Result
Granås, A.G., et al., 2010	- Ethics approval: approved by the Norwegian Social Science Data Service (NSD) and the Regional Committee for Medical Research Ethics - Time horizon: May - September 2006 - Method: The treatment review was based on a structured questionnaire of patients at 23 pharmacies in Norway. The research was conducted in three steps • Recruitment of patients - 73 patients with type 2 diabetes from 23 pharmacies were registered for treatment review - Inclusion criteria: - Male and female patients aged 18 years and over, - get a prescription for a drug or medical device for type 2 diabetes • Treatment review - Pharmacists conducted structured treatment reviews based on the patient's drug profile and patient interviews. - Pharmacists build drug profiles based on electronic records of treatment made at the time of interview based on information provided by patients at the time of the interview. Classification of drugs based on the classification issued by ATC - Interviews included drug use, compliance issues and identification and recording of potential DRP	- 88 DRP were identified from 43 patients out of a total of 73 patients or the equivalent of 1.2 DRP (scale 0-6) - 30 patients were identified as not finding any DRP - There were no statistically significant differences between patients identified by DRP and not related to age and sex - Drug side effects were the most commonly reported related to DRP (22%), Wrong medication or dosage (14%) and the need for additional drugs (10%) - 34% of DRP cases, pharmacists made contact with doctors, but it was not recorded whether the DRP problem could be resolved or not. Direct and written advice is given to patients with 92% DRP - From 637 prescription drugs, 24.3% were drugs that commonly used for the treatment of diabetes (ATC group A10), 8.6% antithrombotic (ATC group B01) 7.7% fat modifying compounds (ATC-group C10) and 5, 5% were beta blockers (ATC-group C07). Statins were prescribed for 49 patients from 67 patients. The majority (95% of patients) were prescribed cardiovascular drugs. The ATC groups that occur most frequently DRPs are drugs used in diabetes (ATC-group A10), fat-producing compounds (ATC-group C10) and beta blockers (ATC-group C07). - 39 from 42 reviews, three or more EG members agreed with the community pharmacist that there was at least one DRP in the examination. 30% of DRP was considered by one EG and community pharmacists have another DRP.

Study	Method	Result
	• DRP and contact with the recipe writer - The DRP category was based on the Pharmaceutical Care Network Europe (PCNE) system adapted to the Norwegian health care system • Evaluation and categorization and problems related to medicine - Evaluation Group (EG) was collected in February and August 2007 - EG was asked several questions to identify additional DRP that were not recorded by community pharmacists. - At the second meeting the results were discussed	
Siaw, M.Y., et al, 20017	- Inclusion criteria: patients in aged ≥ 21 years with uncontrolled T2DM (glycated hemoglobin, HbA1c$> 7\%$). Polypharmacy (use of kronis 5 chronic drugs) and comorbidities (chronic conditions other than diabetes which were classified in the revised ten international classification diseases) - Exclusion criteria: Patients with type 1 diabetes and patients who did not communicate independently - Subjects were divided into 2 groups, with 214 patients included in the intervention group and 197 in the control group. After 6 months, the	- Early sociodemographic and medical characteristics of patients that left the study did not differ significantly from patients who completed the study - During the study no significant danger or undesirable effects were reported in any group - At the beginning of the study, HbA1c levels in the two groups were comparable. In the control group HbA1c levels did not change from baseline to 6 months. In the intervention group when the average HbA1c level was $\geq 8\%$, there was a reduction of 0.8% compared to the control group which only experienced a decrease of 0.2% - The results of the PAID survey after 6 months there was a greater decrease in the intervention group (from 28.6 to 17.1) than in the control group (26.4 to 22.5) - While the results of diabetes patient satisfaction (DTSQ) after 6 months there was an increase from 25.6 to 28.5 in the intervention group and slightly increased in the control group (from 25 to 25.7)

Study	Method	Result
	patients who completed the study were 141 intervention group patients and 189 control group patients - Data collection: Main results included HbA1c, systolic blood pressure (SBP), LDL and triglycerides collected from electronic databases at baseline 3 and 6 months. Secondary results obtained from the survey include problem areas in diabetes / Problem Areas in Diabetes / (PAID) and diabetes management satisfaction / Diabetes Treatment satisfaction Questionnaires (DTSQ). PAID consisted of 20 valid questionnaire items with a 5-point Likert scale from non-issue (0) to serious problem (4). A high PAID score indicated emotional distress. DTSQ was a valid and reliable 8-item questionnaire that measured treatment satisfaction and the perceived frequency of hyperglycemia and hypoglycemia using a seven-point Likert scale from 0 to 6.20. A higher DTSQ score indicated greater treatment satisfaction or worse glucose control.²⁰ - Statistical Analysis: The results of the study were performed chi square test and Mann Whitney U test. All univariate analyzes were followed by multivariate analysis	- The 6-month average cost associated with direct costs for outpatients is US \$ 516.77 for the intervention group and US \$ 607.78 for the control group. Providing interventions can save US \$ 91.01 per patient for 6 months.

Study	Method	Result

DISCUSSION

In the treatment of T2DM, to maintain glycemic control was done by giving various types of drugs with different mechanisms of action. Patients with T2DM are at risk of experiencing drug-related problems (DRP), which could occur at every step during the treatment process and affect the outcome of therapy (13). So we needed the way to identify the problems related to DRP in T2DM patients

Research conducted in Australia successfully developed an evidence-based checklist used to identify DRP in T2DM patients (9). This study showed that the average DRP value was quite high at 4.6 DRP (SD = 1.7) per patient. This showed that the prevalence of DRP in T2DM patients was relatively high, so early identification and resolution of DRP in the management of T2DM patient therapy was very important. High DRP values in T2DM patients were associated with the use of many drugs, so that adequate management of drug use in these patients was needed (9,13).

This DRP potential checklist (PDRP) was the first tool developed by Cally to detect potential DRP in T2DM patients and could be used to detect DRP from patient in data collected previously. Some problems were found from identification using the potential DRP checklist (PDRP) (9). There were 206 times the DRP associated with drug choices with an average of 1.4 drug / patient choice problems. About 60.8% of all patients did not receive antiplatelet despite an increased cardiovascular risk. And nearly half of all patients did not receive lipid-lowering therapy despite high lipid levels (9). Another problem found was the management regimen problem. In patients receiving sulfonylurea therapy, 15 cases (16%) received higher doses than recommended doses. The administration of sulfonylurea at high doses increased the risk of hypoglycemia. Some potential interactions that were identified using the PDRP checklist were related to the use of a combination of ACE inhibitors with sulfonylurea or insulin (44.7%). The use of these drug combinations in managing T2DM therapy required careful monitoring because of the increased risk of hypoglycemia (9).

The identification results also showed 17.6% of the study subjects that had the potential for non-compliance. Improved adherence in T2DM patients contributed to improved glycemic control (9). This PDRP checklist does not

detect potential non-compliance, this information was available from patient data who used self-report tool. Thus, this self-report tool needed to be integrated into the PDRP checklist. An important factor to consider was the PDRP checklist in studying the potential prevalence of DRP and not actual DRP. Therefore, it was necessary to search further study on the clinical outcomes of patients with potential DRP during follow-up, so that the level of clinical significance of the detected DRP can be established (9).

This PDRP checklist can help pharmacists and other health professionals to identify problems in therapy and therapeutic management of T2DM patients (9). This was in line with other studies using different methods. PI-DOC (Problem intervention Documentation) had been used in Denmark as a protocol to identify the presence of DRP (13). In India, clinical pharmacists were involved to optimize patient care by identifying, resolving and preventing drug-related problems (DRP) so doctors must carefully evaluate drug profiles, provide the safest, most effective and simplest treatment regimen to meet individual patient needs (14).

Interventions by pharmacists were always considered as valuable input by the health care community in the process of patient treatment by reducing medication errors, rationalizing therapy and reducing therapy costs. The role of pharmacists in managing T2DM therapy varied including monitoring treatment, operating recurrent prescription services, reviewing medicines for long-term users, giving advice on general management of the condition and participating in local and national health promotion or disease prevention activities (11).

Research conducted in Denmark involved 4th year pharmacy students to collect data relating to DRP in patients with angina pectoris, T2DM and asthma. DRP problems were identified through medication reviews and patient interviews at home. The study found 635 cases of DRP from 155 patients or equivalent to 4.1 DRP per patient, consisting of inappropriate use of drugs, lack of drug monitoring, inappropriate selection of drugs, contra indications not considered in prescribing drugs, drug side effects and problems related to the patient itself such as improper lifestyle and limited patient knowledge about the disease (15). Inappropriate drug which used by patients and other problems (such as limited knowledge about disease, inappropriate lifestyle, fear of treatment, and lack of information) were two of the most common sub-categories of DRP identification in T2DM patients (73%). This high DRP rate occurred because pharmacists who conducted final identification and DRP coding were specially trained, so it was likely to lead to higher levels of DRP identification (15). The high rate of DRP also occurred due to mutual trust between pharmacists and patients when conducting interviews at home, so patients can explain freely the use of drugs properly (15). The intervention was given by pharmacists to reduce DRP can be in the form of providing information. Training for pharmacists to increase

knowledge about DRP was needed so that the role of pharmacists in providing counseling could be based on the patient's perspective. The pharmacist's identification of DRP in pharmaceutical services was the first step followed by steps to resolve and prevent the patient's undesirable therapeutic results. This was in line with other studies conducted in Malaysia on the treatment of dyslipidemia in T2DM patients. Pharmacist interventions had a positive impact on increasing the percentage of T2DM patients who achieve treatment goals compared to patients treated with treatment without pharmacist intervention. The detailed academic explanation program showed the positive impact on the prescribed statin therapy. Some factors that need attention were the number of academic details, attendance of follow-up periods, and sample sizes from health care providers and patients (16).

Other research on the need for multidisciplinary collaboration in the management of patients with chronic diseases had been carried out in India and Pakistan in diabetic patients with poor cardio metabolic profiles. The multicomponent QI strategy applied was associated with twice the likelihood of achieving the goals of combined diabetes care and greater baseline-to-EOS reduction for each risk factor compared to usual care. Intervention participants showed improvement in HRQL and treatment satisfaction, which indicated that they did not object to the intensity and extra follow-up of the intervention (17).

Similar research was also carried out in Singapore, which was a country with three major ethnic groups namely China, India and Malay. This study showed a difference between the usual T2DM patient treatment and the collaborative treatment group. Compared with usual care, average reduction in HbA1c was up to 0.8% that was observed in patients in the multidisciplinary collaborative treatment group with poorer baseline controls. Poor glucose control was often caused by inappropriate use of drugs and lack of follow-up; therefore, closer monitoring by clinical pharmacists provides timely drug optimization. Additionally, clinical pharmacists in this study were trained to use the SIGN algorithm specifically designed for Asian patients who refused to use glucose measurements, and active insulination. Titration was still done despite low SMBG compliance. Because of the intervention of this clinical pharmacist, patients in the multidisciplinary collaborative treatment group got benefit from glycemic improvement because each level of improvement in HbA1c will reduce the risk of diabetes-related complication (12).

In addition, patients in the multidisciplinary collaborative treatment group experienced decrease in diabetes-related pressure and greater satisfaction with their treatment. This treatment approach allowed pharmacists, nurses and dieticians to spend enough time to provide diabetes education and counseling individually. They were also able to increase patient confidence and knowledge, and empowered patients also tended to achieve a better quality of life and higher

satisfaction with diabetes treatment. In the 6-month study, patients who received targeted educational interventions and were provided by a multidisciplinary care team had improved quality of life (HUI3, I: 0.02 vs C: 0.003; $P = .03$) and satisfaction with diabetes care (I: 3.59 vs C: -5.61; $P = .001$) (12)

In addition, the inclusion of a multidisciplinary treatment team also alleviated the workload of doctors. Therefore, doctors spented more time with other patients, who may be more acutely ill or needed immediate attention, while the role of clinical pharmacists was expanded in counseling, monitoring and optimizing the drug causing improvements in the overall quality of patient treatment.

The total gross outpatient costs associated with diabetes incurred per patient for 6 months in this study were 15.0% less in multidisciplinary collaborative treatment than usual care. Similarly, one study showed a 7.8% -21.9% reduction in total direct costs for patients with diabetes who received pharmacist's consultation in an outpatient setting over 2-year period. Cost savings (US \$ 91.01 per patient) were comparable to 6-months study in the United States, which found savings about US \$ 84.00 per patient. The cost savings observed in this study were associated with lower treatment costs in patients who were managed by a multidisciplinary treatment team. When pharmacists were actively involved in patient treatment, research had revealed cost savings as a result of closer therapeutic monitoring and replacement of branded medicines with generics. Conversely, treatment costs may be higher in usual treatment settings. Because of the lack of a thorough assessment of drug use and hence, patients who failed to achieve clinical targets were advised to switch to, or added other drugs, no needed for more expensive drugs.

This finding served as direct evidence in evaluating multidisciplinary collaborative treatment in Asia and can be enhanced by estimating indirect costs. Finally, because of differences in patient populations, research designs, health care systems and the practice of privileging health professionals throughout the study, direct comparison with other studies were not possible. However, the control group in this study served as a good comparison to illustrate the impact of multidisciplinary collaborative treatment.

A team-based approach consisting of doctors and clinical pharmacists along with other health professionals was key and had the potential to meet the complex needs of many diabetic patients including patient drug therapy (18). This approach was carried out by designing a comprehensive drug management service that allowed pharmacists to play more active role in helping to manage diabetic patients. Pharmacists worked closely with patients and other health professionals in designing, assessing, implementing and monitoring therapeutic plans that help patients achieve positive clinical outcomes. When this service was

provided, patients received standardized patient treatment that focused on identifying, resolving, preventing drug-related problems (18).

IV. CONCLUSION

Multidisciplinary collaborative treatment supported the effectiveness of this approach in managing chronic diseases. Pharmacist interventions helped to improve the quality of treatment and reduced health care costs. Patient education and counseling by pharmacists in identifying and resolving drug-related problems (DRP) and improving treatment compliance could help to achieve the goals of managing diabetes mellitus therapy

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