



# Implementation of the Package of Essential Non-Communicable (PEN) Disease Interventions in Low-Resource Settings: A Systematic Review

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## Abstract

**Background:** To deal with the rising prevalence and death rate of non-communicable diseases, the WHO designed a package of essential interventions for non-communicable diseases for low- and middle-income countries. This review aimed to identify the barriers and facilitators of the implementation of this program.

**Methods:** The electronic databases of PubMed, Scopus, Web of Science, Cochrane Library, and Scientific Information Database (SID) were searched for papers without a time limit at the end of Dec 2020. Only English and Persian languages were considered. The PRISMA guideline was consulted.

**Results:** Overall, 15 articles were selected for the final analysis out of 404 initially retrieved ones, based on inclusion/exclusion criteria and quality assessment. Thirteen articles had good quality, while 2 articles were of fair quality. Studies were published during 2014-2020. Thematic analysis was used to make sense of papers so that barriers and facilitators were categorized within 2 main themes and 7 sub-themes. Certain organizational factors including human resources, service delivery, structure, leadership/governance, data and information, resources, and financing were identified as barriers and facilitators. Knowledge and culture, and economic and social factors were identified as contextual factors.

**Conclusion:** By considering the factors identified in this study, policymakers and health system managers can be more successful in implementing this WHO PEN and similar packages.

**Keywords:** Non-communicable diseases; Primary health care; Low-resource settings

## Introduction

One of the challenges of health systems is the rising prevalence of non-communicable diseases. The proportion of deaths associated with non-communicable diseases is projected to increase from 59% in 2002 to 69% in 2030 (1). NCDs are

responsible for the deaths of 41 million people annually, which accounts for 74% of global fatalities. Around 17 million individuals die from an NCCD before they reach their 70th year old; 86% of these



premature deaths occur in low- and middle-income countries. Low- and middle-income countries have a 77% mortality rate due to NCDs. NCD deaths occur more frequently in cardiovascular diseases, with 17.9 million deaths annually, while cancers and chronic respiratory diseases account for the majority (4.1 million), and diabetes causes the most deaths (2.0 million including kidney disease deaths caused by diabetes). These four diseases are responsible for more than 80% of all premature deaths caused by NCDs.(2, 3)

Hypertension and diabetes are the most common conditions that significantly contribute to the burden of non-communicable diseases. Therefore, the WHO designed the Package of Essential Non-communicable Disease (NCDs) Interventions for Primary Health Care should begin to prevent heart attack, stroke, and kidney disease through integrated management of hypertension and diabetes. Once primary healthcare workers develop the skills to implement effectively the protocol, the portfolio can be expanded to other NCDs (4).

Package of Essential Non-communicable Disease Interventions for Primary Health Care (WHO PEN) sets minimum standards for the management of non-communicable diseases. Thus, its implementation leads to strengthening the national capacity to integrate and scale up care for heart disease, stroke, cardiovascular risk, diabetes, cancer, asthma, and chronic obstructive pulmonary disease in primary health care in low-resource settings (5).

The purpose of the package is to provide an equitable framework for initiating action to develop primary care in countries that strive to achieve universal access to the health sector. Therefore, the WHO PEN should be an integral part of pro-poor health care programs that target vulnerable and disadvantaged groups. As noted, the package should be considered as a set of minimum standard interventions and only as a starting point for action to address NCDs in primary healthcare in restricted-resourced areas (5).

There is little global evidence about the implementation and effectiveness of these interventions in the areas where this program is implemented, and

the little available evidence has conflicting results (6, 7). The findings of this review, to identify global experiences on the implementation of this WHO PEN, can provide useful information to the health sector policymakers to identify and eliminate the gaps and resolve the challenges of this policy as well as deal with chronic diseases through any national policy.

## **Methods**

The protocol of this review is registered in PROSPERO( *CRD42021256242*).

### *Types of Studies and Data Sources*

A systematic literature search of PubMed, Scopus, Web of Science, Cochrane Library, and Scientific Information Database (SID) was conducted without a time limit at the end of Dec 2020. Google Scholar was also used for citation track chasing.

### *Search strategies*

The search strategy involved systematic use of keywords in various combinations. To find relevant articles, general keywords were selected (“Noncommunicable Diseases” (MeSH), “NCD”, “Non-communicable Diseases”, “Non communicable Diseases”, “Chronic Diseases”, “WHO-PEN”, “WHO PEN”, “PEN”, “Non-infectious Diseases”, “Non infectious Diseases”, “Noninfectious Disease”, “Non-communicable Chronic Disease”, “Non-infectious Disease”) combined using the AND and OR operators to ensure a comprehensive and complete search process. Detailed search strategy including electronic search strategy for at least one database is shown in supplementary file1.

### *Eligibility (inclusion and exclusion) criteria*

The present systematic review included articles that were written in English and Persian language. As we aimed to include only original studies and cross-sectional studies resulting from studies related to the WHO PEN package, any type of other

studies including review articles, letters to the editor, and commentary/perspective articles, were excluded.

### Data collection process

According to the search strategy of each database, articles were extracted and imported into the End-Note software (V.X8), and duplicate articles were removed. Then two independent reviewers (AA and MA) screened the articles based on the title, abstract, and full text. If the two reviewers disagreed, the third reviewer's opinion was used. Furthermore, the reevaluation of the full-text article was performed based on inclusion and exclusion criteria.

### Quality Assessment of Studies

The quality of articles was evaluated by using the Consolidated Health Economic Evaluation Reporting Standards (CHEERS), Appraisal Tool for

Cross-Sectional Studies (AXIS), Critical Appraisal Skills Programme (CASP), and Mixed Methods Appraisal Tool (MMAT) for assessing Economic Evaluation, Cross-Sectional, Qualitative and Mixed Methods studies.

To evaluate the quality of studies, special tools were used according to the type of study. Studies were scored based on four groups (Table 1). For example, cross-sectional studies with a score of 20-16 were in the category of good-quality studies and economic evaluation studies with a score of 24-20 were in this group. Studies belonging to the average or below-average quality assessment group were excluded from the study and 15 articles remained (Table 2). To reduce bias, the quality of the articles was assessed by two independent evaluators, and disagreements were discussed and resolved.

**Table 1:** Four groups of study quality assessment criteria

	<i>Variable</i>	<i>AXIS</i>	<i>MMAT</i>	<i>CASP</i>	<i>CHEER</i>
1	Good	20-16	20-16	10-8	24-20
2	Fair	16-12	16-12	8-6	19-17
3	Average	12-8	12-8	6-4	16-14
4	Below average	8-4	8-4	4-2	13-11

### Data Extraction

After the qualified papers were determined, data were extracted based on an extraction form, that encompassed authors' information, publication year, type of study, study setting, study objectives, methodology, results of actions, and key findings. To critical appraisal and improve accuracy, data extraction was conducted by independent researchers, and disagreements between researchers (AA and MA) were resolved through discussion.

### The method for thematic analysis

Braun & Clarke's six-phase framework was used to guide thematic analysis. 1) Become familiar with the data, 2) Generate initial codes, 3) Search for themes, 4) Review themes, 5) Define themes, 6) Write up (8).

### Results

Overall, 404 articles were extracted through database searches. Search results from each database were stored in EndNote X8 and 62 duplicate articles were removed. By screening the title and abstract based on the inclusion and exclusion criteria 291 papers were also excluded. In the last step, 51 full-text articles were assessed for the eligibility criteria, and 16 articles were included. After quality assessment, one more article was excluded and 15 articles were included for the final analysis. Of the 15 articles included in the study, the quality of 13 articles was good, and 2 articles were fair. Fig. 1 shows the steps for selecting articles based on the PRISMA flowchart.

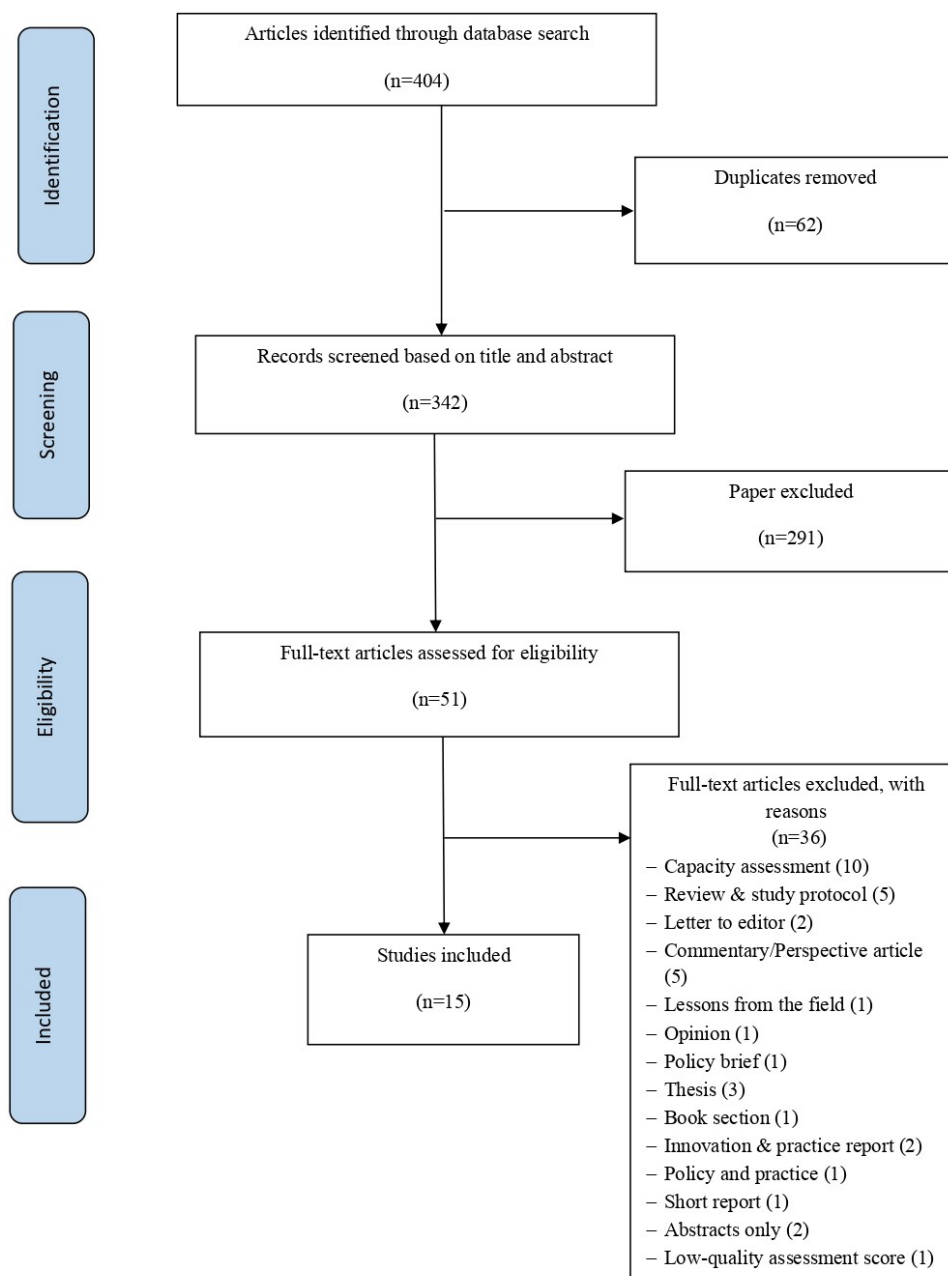


Fig. 1: PRISMA flowchart for study inclusion

### Characteristics of the included studies

The characteristics of the included studies (7, 9-22), are displayed in Table 2. There were 15 studies published during 2014-2020. Six studies were conducted as performance evaluation studies

(7,9,11,13,16,19), 3 studies were conducted as economic evaluation of the WHO PEN package (10,20,21), 4 studies were conducted as qualitative studies (12,14,15,18), and 2 studies were conducted as the mixed method (17,22).

Table 2: Characteristics of the included studies

<i>Authors (year)</i>	<i>Location/ Setting</i>	<i>Study design</i>	<i>Aims of the study</i>	<i>Finding/Effectiveness/Impact</i>	<i>Quality Rating of Study</i>
1 Dukpa et al (2015)(10)	Bhutan	A model-based economic evaluation	Assessing the cost-effectiveness of the PEN project implemented in Bhutan and analyzing the costs and health consequences of the program in both the short and long term.	The results support the WHO's standpoint, which indicates that the WHO PEN is very cost-effective and feasible to implement in all countries.	Good
2 Wangchuk et al (2014)(7)	Bhutan	A performance assessment study	The performance of the PEN project in detecting and managing non-communicable diseases (NCDs) and their risk factors was assessed.	Implementation of the PEN intervention in the primary healthcare setting of Bhutan led to improvement in blood pressure and diabetes control and a reduction in CVD risk.	Good
3 AlHelo et al (2019)(11)	Gaza/Palestine	A cross-sectional study	To evaluate the impact of these interventions in reducing cardiovascular disease risk as these interventions are newly implemented.	There was no statistically significant difference between pre- and post-parameter interventions for systolic and diastolic blood pressure, waist circumference, weight, body mass index, and cholesterol, as well as for tobacco use and cardiovascular risk ( $p > 0.05$ ). In contrast, fasting blood sugar was lower, with a statistically significant difference ( $p = 0.049$ ).	Good
4 Gyamfi et al (2020)(12)	Ghana	A qualitative study	To identify and describe the community health nurses' (CHNs) perceptions of facilitators and challenges faced with TASSH implementation.	Three themes emerged following deductive analysis using the Consolidated Framework for Implementation Research, including (1) Patient health goal a setting-relative priority and positive feedback from nurses; (2) Leadership engagement; (3) Availability of resources, with limited space and personnel time to carry out TASSH duties, limited blood pressure (BP) monitoring equipment, and transportation, listed as barriers to effective implementation.	Good
5 Hadavand Siri et al (InPersian)(2020)(13)	Iran	A cross-sectional study	To examine the client's adherence to the visitation schedule recommended by health centers in Ir-PEN, based on their cardiovascular risks.	Adherence was low in all four evaluated cities. The overall adherence rate was 19.73% in this study, and timely referral was higher in women than men (21.98% vs. 16.37%).	Good
6 Etemad et al (2016)(14)	Iran	A qualitative study	To determine the challenges of implementing this package in Iran's healthcare system.	The findings were categorized into nine groups of challenges, including management, organizational, functional, intelligence, political, demographic, economic, cultural, and educational	Fair
7 Tahir Ahmed et al (2019)(23)	Iraq	A cross-sectional design	To explore the factors that affect the weak response of attendants to primary health care centers for the diagnostic second visit following the first screening one.	The factors affecting adherence are as follows: 1. Socioeconomic as long-distance from treatment settings, 2. Health care workers related factors, such as a lack of knowledge	Below average

Table 2: Continued ...

8	Collins et al (2017)(15)	Kyrgyzstan	The qualitative evaluation	To identify opportunities to improve the implementation of PEN in Kyrgyzstan.	of health professionals about the program, <sup>3</sup> . The nature of the illness and 4. Patient-related factors. Qualitative analysis found 11 themes that seemed to help explain the quantitative findings. Themes include mainstreaming of PEN protocols, use of lifestyle interventions, training for PEN protocols, understanding and use of cardiovascular risk charts, use of drug treatment, lack of human resources, lack of educational materials for patients, population health promotion campaigns, modern technologies, patient demographics, access to risk estimation.	Good
9	Laatikainen et al (2020)(16)	Moldova	A cross-Sectional study	To determine the feasibility of implementing and evaluating the WHO PEN approach in primary healthcare in the Republic of Moldova.	It is feasible to implement and evaluate interventions for the prevention of CVD in the Republic of Moldova using routine clinical data from paper-based records.	Good
10	Aye et al (2020) (17)	Myanmar	A sequential explanatory QUAN-QUAL mixed methods design	To assess the implementation of PEN, and its effectiveness, and understand the facilitators and barriers in its implementation.	High loss to follow-up, poor recording of CVD risk score, and lack of essential medicines and equipment were the key challenges identified that need to be addressed before further expansion of the PEN project to other townships.	Good
11	Rawal LB, et al (2020) (18)	Nepal	A qualitative study	To explore the barriers and facilitators to engaging community health workers (CHWs) for NCDs prevention and control in Nepal.	Some challenges and barriers were identified, including inadequate NCD training, high workload, poor system-level support, inadequate remuneration, and inadequate supply of logistics and drugs. The facilitating factors included government priority, formation of NCD-related policies, community support systems, social prestige, and staff motivation.	Good
12	Agrawal, et al (2018) (9)	Nepal	A cross-sectional study	To evaluate the care delivery in diabetes patients in a rural primary care hospital that had implemented the WHO PEN protocol.	The results revealed adherence to the PEN protocol and identified several areas of improvement in diabetes care delivery in rural hospital functioning. The results reflected the need for regular CME programs on diabetes for our team of healthcare providers.	Good
13	Kontsevaya et al (2017) (19)	Kyrgyzstan	A cross-sectional study	To compare the inputs, outputs, and outcomes for PEN pilot sites versus non-PEN pilot sites in Bishkek city for 12 months; To assess the possibility of and perspectives for developing an approach to the economic evaluation of PEN implementation in Kyrgyzstan	The evaluation in PEN centers did not show clear and significant evidence of a real impact resulting from the implementation of the PEN protocols on primary care, so there were no arguments for performing a long-term economic analysis of the combination of the effects and costs.	Fair

Table 2: Continued ...

14	Basu et al (2019) (20)	South Africa	A microsimulation and cost-effectiveness analysis	To assess how cardiovascular risk factors are distributed across sub-populations and to identify which cardiovascular treatments should be prioritized. To investigate whether implementation of either guideline would lead to a reduction in premature mortality	Implementation of South Africa's Primary Care101 guidelines averted slightly more overall DALYs and had better cost-effectiveness than implemented of the WHO PEN guidelines.	Good
15	Rattanavipapong et al (2016) (21)	Indonesia	Model-Based Economic Evaluation	The objective of the quantitative assessment is to evaluate the cost-effectiveness of the PEN program compared to a "no screening" policy choice.	Providing the current PEN policy had the greatest health benefits in terms of the lowest DALYs lost or highest DALYs averted compared to no screening. In addition, adopting policy option 2 requires a slightly lower budget for the first year compared to the current policy (the PEN program)	Good
16	Collins et al (2017) (22)	Jordan	A mixed method	to identify opportunities to improve total CVD risk-based guidance for humanitarian settings.	Few patients had a documented and correct CVD risk score, and half of high-risk patients were not prescribed lipid-lowering treatment. The qualitative analysis found nine themes.	Good

Finally, by conducting the thematic analysis of the articles, 2 main themes and 7 sub-themes were identified, and for each sub-theme, effective factors including facilitators and barriers to the successful implementation of WHO PEN were identified discussed as follows (Table 3).

### *Internal organizational factors*

#### *Human resources*

In this theme, most of the articles refer to employee training. In Iran, Nepal, and Myanmar, lack of appropriate and sufficient training (7, 14, 18) has been recognized as one of the barriers to the implementation of this program. Moreover, in a study conducted to improve the implementation of this program in Kyrgyzstan, one of the eleven themes discovered in the study was the lack of systematic training for new employees (15). In other studies, not achieving health education goals (22) and financing educational needs (20) were among the barriers to implementing this program.

Another effective factor in this theme is the motivation and desire and job satisfaction among employees to provide services to clients (9, 18). The feedback from patients about the effect of this program on their health plays a key role in creating motivation and high willingness of staff (12).

### *The delivery of healthcare services*

This category is related to the way of providing services and following WHO PEN protocols. Some studies reported non-adherence to the WHO PEN protocols (15, 17, 22). In Ghana, integrating new tasks with other routine tasks and responsibilities has been difficult for some nurses (12). Failure to provide timely services and the non-availability of free essential drugs in the healthcare center (18) are also other problems and barriers on the way to providing services based on the WHO PEN protocols.

Increasing awareness of non-communicable disease management, referral criteria, and use of monitoring tools (11) is one of the influencing factors on how the delivery of healthcare services. Planning to improve the participation of nurses in counseling (15) will be an effective factor. Barriers in this field have been reported as the tendency to provide lifestyle intervention services as the first line of treatment, contrary to the protocols (15, 22). In addition, among the other barriers was the limited understanding of physicians regarding the use of treatment protocols at the level of primary prevention (22).

**Table 3:** Main themes of facilitators and barriers to the WHO PEN implementation

<i>Theme</i>	<i>Sub-theme</i>	<i>Effective factors</i>	<i>Facilitators and Barriers</i>	
Internal organizational factors	Human resource	Education & training motivation	Facilitators	
	Providing services	Job Satisfaction Adhere to program protocols Unit process and feedback Lifestyle interventions Risk assessment protocol referral system Patient follow-up visits	Facilitators	
	Structure	Suitability of health system structure with the needs of non-communicable diseases Expanding the scope of the program Health system readiness Up-to-date health system Strengthen PHC	Facilitators	
	leadership/Governance	Too much bureaucracy Government's commitment and consideration of health benefits in government policies Consulting with implementation science experts Cooperation between related ministries and in- terdepartmental cooperation Support managers and leaders Program priority for the Ministry of Health Sustainability at managerial and executive levels and short-term management period Expert support for management decisions	Barrier Facilitators	
	Data and information	Haste in planning Completeness of information Reliable data	Barrier Facilitators	
	Resources and Financing	Lack of systematic registration and reporting Shortage of capacity and resources in primary care centers High cost of care for NCDs and increased cost of treatment Increasing the unbearable costs of patients pay- ing out-of-pocket	Barrier Barriers	
	External organiza- tional factors	knowledge and culture, Economic and social factors	Low cost of preparation and implementation Providing free services Insurance	Facilitators
			Access to health facilities More use of services by women The importance and priority of health for the pa- tient	Facilitators
			Acceptance of the program by most patients Gender restriction	Barriers
			Lack of trust in healthcare providers Non-cooperation of clients	

Referral of patients outside of the WHO PEN protocols due to lack of resources and capacity in primary healthcare centers and the inefficiency of the existing referral mechanism, well as, the insufficient referral mechanism and the lack of a systematic approach to refer and follow patients from

one health center to another were among the other problems of referral in this program (18).

In the field of risk assessment protocols of this program, one of the major problems is reported the inability of employees to perform the risk assessment (15, 17, 22). Practical barriers to receiving risk assessment services such as long distances



and possible difficulty of traveling to healthcare centers (15) have been stated among other things related to providing risk assessment service.

Compliance with regular follow-up of patients in the WHO PEN protocols (17, 18), was one of the factors affecting the successful implementation of the program. In Bhutan, only 10% of patients missed their treatment follow-up visits (7). In Nepal, about 13% failed to follow up, this could be due to migration of patients, social stigma due to chronic drug use, and death (9).

#### ***The structure***

In general, the readiness of the health system to reduce the increasing burden of non-communicable diseases, (18) the proportion of the structure of the health system with the needs of non-communicable diseases, (14) strengthening the PHC system (11) and the need to expand and develop PEN WHO intervention throughout the country, (17, 18) are the factors reported in this theme.

#### ***Leadership/ Governance***

Studies reported certain factors that worked for the implementation of the WHO PEN including the high level of commitment of the government (14, 18), considering health benefits in government (14), and the development and implementation of policies and programs related to non-communicable diseases (18), the high priority of prevention and control of non-communicable diseases for the Ministry of Health (18), the need for cooperation with other relevant ministries and related sectors other than health sector (18), the inter-sectoral coordination (14), and the importance of continuous guidance from the implementation science experts (12), the support of leaders or managers of health centers (12, 15), and creating the media campaigns to improve the health of the population (22).

#### ***Information***

Barriers that were reported in the field of data and information, included the unavailability of systematic reporting and recording systems (17, 18), lack of comprehensive information and of data dealing with patients with NCDs at the health facility (14, 17, 20), and lack of reliable data (20).

#### ***Resources and Financing***

In Indonesia, providing the current PEN policy had the greatest health benefits in terms of the lowest DALYs lost or highest DALYs averted compared to no screening (21). In Bhutan, the current PEN program and universal screening are certainly cost-effective and show they were cost-saving interventions (10). According to studies, availability of insurance (14), provision of care, medication, and free equipment (11, 17), low costs of preparation and implementation of PEN compared to non-implementation, cost savings, and cost-effectiveness of PEN implementation will be among the facilitators of the implementation of this program (10, 19-21).

Lack of internal resources and capacity, for example, trained human resources, regular supply of drugs, appropriate equipment, logistics-related challenges such as lack of adequate space, lack of furniture, and time, is a commonly reported barrier (9, 11, 12, 15, 17, 18). Due to the high costs of care for non-communicable patients (18, 20) financial resources instability and economic sanctions (14), and budget volatility (20), financing this program will be a challenge. Increasing costs of treating hypertension and dyslipidemia (20), as well as lack of timely supply and availability of free essential drugs at the health center, forces patients to purchase NCD drugs from private pharmacies and as a result, it adds to the unbearable out-of-pocket costs of patients (18).

#### ***External organizational factors: knowledge, culture, and economic and social factors***

This theme includes things that are rooted in the knowledge and awareness and culture of patients and people covered by health centers. In this regard, the facilitators reported by studies in this field include the need to inform and increase public awareness (14, 15), motivate acceptance of interventions by most patients (12), promote the use of services by women (7, 16) and increase adherence of women to regular visits (13), and increase the importance and priority of health and its consequences for patients (12). On the other hand, in some countries, women have more challenges

than men in sports due to gender, cultural, or security restrictions (14, 22).

Studies have shown different barriers and challenges including lack of cooperation by clients for receiving care (12), non-adherence of high-risk patients to drug interventions (22), not following referrals to specialist practitioners in patients (17), lack of interest or ability to exercise (22), as well as patients' self-report of their condition, which may lead to overestimation or underestimation of treatment levels due to social acceptability bias (20), can under the program in achieving its goals (15). Overall, barriers to access to health care including culture, trust, and financial implications of care in the poor (20), transportation problems and associated costs for patients and clinic staff (9, 12), missed follow-up visits due to the inability to walk long distances by elderly, disability following stroke and reluctance to travel by bus due to motion sickness (7), and the patients' spiritual beliefs determine their response to the disease and the strategies they use to deal with it. For example, the patient believed that accepting she had hypertension would accelerate her death (12), mistrust of health care providers (22), patients' embarrassment from full disclosure of psychological, social, or occupational background, were also among the barriers to implementation of the WHO PEN (22).

## Discussion

Using the thematic analysis of the articles, this review summarized the facilitators and barriers to the WHO PEN implementation reported over the past 10 years. As a result of this analysis, certain organizational factors including human resources, service delivery, structure, leadership/governance, data and information, resources, and financing were identified from the studies. knowledge and culture, economic and social factors were identified as beyond organizational factors.

Employee motivation has been identified as one of the factors affecting this program. Many studies have been conducted in the field of job motivation of human resources working in the health sector

(24). The results of some studies emphasized the importance of internal factors and others emphasized the importance of external factors (25, 26). Lack of internal resources and capacity is a commonly reported barrier. Little information is known about the capacity of PHCs (Primary health care) in LMICs (Low- and middle-income countries) to meet the needs of people with NCDs. Although NCD interventions (e.g., diagnosis and treatment) are universal, effective care delivery strategies for people to access common socioeconomic, cultural, and health scenarios differ in LMICs compared to high-income countries (27).

One of the other factors affecting the implementation of the PEN program is the training of employees (28). Comprehensive training and development programs can help to focus trainees on skills, attitudes, and knowledge to achieve goals and create competitive advantages for the organization (29). Many studies have revealed the impact of training on organizational performance (30-33). Effective service delivery in compliance with PEN program protocols will play a role in its successful implementation. healthcare delivery means providing effective services to people with diseases for which there are proven treatments (34). Well-designed healthcare delivery systems are powerful resources for economic development (34).

Another effective factor identified in this study is the structure of the health system to face the crisis of non-communicable diseases. Weak regulatory structures have been identified as one of the barriers to effective surveillance of non-communicable diseases in low- and middle-income countries (35).

The reviewed studies reported leadership and governance as factors influencing the implementation of this program. One of the most important and vital factors for the successful completion of projects is the support of senior management (36, 37). Many researchers also agree that top management commitment is critical (38-42). Senior management must not only demonstrate commitment and leadership but also must strive to create interest in

implementing and communicating change to everyone in the organization (40).

### Strengths and limitations

This study has a protocol registered in PROSPERO, which is an international database of prospectively registered systematic reviews in health and social care, which increases the validity of the results. The review provides novel findings that can inform the design of future studies on the implementation of this WHO PEN package and its impacts. Moreover, the assessment of review quality was used to assign the strength of evidence to the findings. This systematic review has some limitations. Although five well-known databases were used, only studies in English and Persian studies were included in this review.

### Conclusion

The effective factors that include facilitators and barriers to the implementation of this program are divided into two groups, external and internal organizational effective factors, and most of the factors identified in the studies are related to internal organizational factors. The study identified and explained the factors influencing the implementation of the program (WHO PEN) that facilitate the successful implementation of this program, or the barriers to its implementation to support its successful implementation in primary healthcare requires that they be removed. Therefore, according to the effective factors identified in this study, policymakers and managers of the health system will be more successful in implementing this package (WHO PEN).

### Journalism Ethics considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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### Conflict of interest

The authors declare that there is no conflict of interest.

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