International evidence-based guidelines on hypertension and type 2 diabetes mellitus: A systematic review

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Abstract

This systematic review provides a high-quality, comprehensive summary of recommendations on hypertension (HT) and type 2 diabetes mellitus (T2DM), accentuating patient blood pressure, HbAIc levels, patterns of drug treatment, management, and screening of these diseases. The overall objective of the review is to support adapting existing clinical practice guidelines in Indonesia, Vietnam, and Myanmar. The database PubMed and the web search engines Google and Google Scholar were searched from October to December 2019 for evidence-based guidelines covering the overall disease management in Europe, the United States of America, and low and middle-income countries (Indonesia, Vietnam, and Myanmar-IVM later on). Nine studies were selected for the review, seven concerning HT and five T2DM. Guidelines in IVM and Europe identified HT as increased blood pressure (BP; \geq 140/90 mmHg). IVM guidelines also recommended commencing drug treatment if lifestyle interventions were not successful. Four international HT guidelines recommended monitoring BP every few months, and the other three guidelines gave recommendations based on the patient's current BP levels. All five T2DM guidelines recommended target HbA1c levels below 7%-6.5%, but only IVM guidelines included re-examination every 3-6 months. Metformin was recommended as the first choice of medical treatment, if not contraindicated. Amid the guidelines' recommendations, there were no major variations in the Class of recommendation and Level of evidence (except IVM guidelines where COR and LOE were missing). Revision and completion of IVM guidelines by this grading system would enhance evidence-based and informed decisions in clinical care.

Keywords

Systematic review, guideline, hypertension, type 2 diabetes mellitus, Asia

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Introduction

Non-communicable diseases (NCDs) present a major burden on health, healthcare systems, and development globally, as they cause premature deaths, thus economically affecting nations and their individuals.^{1,2} These diseases, particularly cardiovascular diseases, chronic respiratory diseases, diabetes mellitus, and cancer, are leading causes of mortality in the South-East Asia Region, with an estimated 9 million deaths each year.³ Key elements in decreasing the occurrence of NCDs are early detection, screening, and treatment.² The most effective way to manage non-communicable diseases is to reduce the risk factors largely attributable to them, such as hypertension, diabetes mellitus, and stroke.^{4,5}

The review was developed as a part of the EU Horizon 2020 SUNI-SEA project, which is being implemented in

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Source	Access date	Search terms
PubMed/Google/ Google Scholar	01/10/2019	 ((((((((((((((((((((((((((((((((((((

Table I. Search algorithms and key words.

Indonesia, Vietnam, and Myanmar (IVM). Scaling-Up Noncommunicable Diseases Interventions in South-East Asia (SUNI-SEA) is an international project with the goal of verifying effective approaches to non-communicable diseases, extending evidence-based HT and T2DM prevention and treatment programs, and strengthening the provision for HT and T2DM prevention and management services. The project aims to provide evidence to achieve sustainable development goals, all based on experiences in Southeast Asian countries.⁶

Hypertension (HT) is highly prevalent throughout the world, with the scale of increase of NCDs particularly observable in Southeast Asia.⁷ Studies currently report the prevalence of HT to be around 35% and is accountable for approximately 1.5 million deaths annually.^{8,9} A much higher percentage is attributed to the lack of awareness and control of raised blood pressure for all people in the Southeast Asia Region, being nearly 50%.⁷ In population-based studies, the prevalence of HT in Malaysia in 2011 was estimated at 43.5% (\geq 30 years), in Myanmar in 2009 at 30.1% (15–64 years), Sri Lanka between 2005 and 2006 at 23.7% (\geq 18 years) and in Vietnam from 2002 to 2008 at 25.1% (\geq 25 years). The prevalence of HT in Indonesia has not been thoroughly explored due to the lack of data on adults (15 years and older).⁷

The Southeast Asia Region faces a diabetes epidemic, too.¹⁰ Of the diabetic population, more than 85% suffer from type 2 diabetes mellitus (T2DM).¹¹ The prevalence of diabetes in South Asians is four times higher than in any other ethnic group owing to the individual susceptibility to T2DM.¹² Nevertheless, roughly 57% of the cases are undiagnosed.¹³ The estimates of the prevalence of diabetes in adults range from 4.0% in Nepal to 8.8% in India. An increasing proportion of obese and overweight children and adolescents have led to an increased risk of T2DM.¹⁴ Of particular concern is the additional number of deaths and the economic burden due to diabetes. Based on the latest statistics, patients pay between 43 and 870 USD to treat the disease and its complications.¹¹

Both HT and T2DM are preventable conditions and are commonly associated with an unhealthy lifestyle, a lack of physical activity, and the harmful use of tobacco and alcohol.¹⁵ Therefore, it is imperative to produce and use evidence-based recommendations based on the best local and international evidence. The adaptation of recognized international recommendations from clinical practice guidelines for the specific environment in communities in Southeast Asian countries is addressed by international teams of the project SUNI-SEA with the aim of developing interventions tackling NCDs with the necessity of adjusting to local needs and requirements.

The overall objective of this systematic review is to propose modifications in existing guidelines in Indonesia, Vietnam, and Myanmar based on identified differences in the diagnosis, management, and treatment of HT and T2DM from current international evidence-based guidelines' recommendations for these non-communicable diseases. The systematic review was conducted as a part of an EU-funded SUNI-SEA project. No ethical constraints were identified.

Methodology

A computerized literature search was initiated on publications from January 1, 2010 to December 31, 2019 and executed primarily within the PubMed database. This database offers free full-text biomedical and life sciences journals. The search was conducted from October to December 2019, using a combination of keywords and relevant subject headings related to HT, T2DM, guidelines, and recommendations. The search was complemented with browsing the web for determining pertinent publications (Table 1). The guidelines were searched in close collaboration with all SUNI-SEA project partners.

Selection criteria for the systematic review included guidelines for two non-communicable diseases—HT and T2DM—containing the Class of recommendations and Level of evidence, and that the publication originated either from Europe, the United States of America, or low and middle-income countries (focusing on IVM). Attempts were made to recognize and translate non-English language papers. Guideline publications only qualified for the systematic review if they had been fully published and not older than 10 years.

The authors of this article individually selected suitable publications based on the criteria and extracted all necessary

Reference				
number	Study author(s)	Year	Area/country	Type of guideline
I	Arnett et al. ¹⁶	2019	United States of America	Primary prevention of cardiovascular disease
2	Williams et al. ¹⁷	2018	Europe	Management of arterial hypertension
3	Whelton et al. ¹⁸	2017	United States of America	High blood pressure in adults
4	Perk et al. ¹⁹	2012	Europe	Cardiovascular disease prevention in clinical practice
5	World Health Organization ²⁰	2018	World (Myanmar)	Noncommunicable disease interventions
6	Soelistijo et al. ²¹	2019	Indonesia	Management and prevention of T2DM
7	Vietnam Ministry of Health ²²	2017	Vietnam	Diagnosis and treatment of T2DM
8	Indonesian Society of Hypertension ²³	2019	Indonesia	Management of HT
9	Vietnam Ministry of Health ²⁴	2019	Vietnam	Diagnostics, treatment, and management of some non-infective diseases

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data. All discrepancies were discussed and solved. The total number of selected guidelines concerning non-communicable disease was 9 (HT—7; T2DM—5), with some of the included guidelines covering both topics. The oldest guideline included in this review was published in 2012. In the results, we present the recommendations for HT and T2DM separately, thus guidelines 1–5 and 8–9 for HT, and guidelines 1 and 4–7 for T2DM. Table 2 presents the characteristics of the reviewed studies.

Subsequently, the following information, targeted at the prevention and treatment of HT and T2DM, was obtained from each guideline: guideline authors, year of publication, the Class of recommendations, and Level of evidence.

A total of 367 publications, including guidelines, recommendations, or their reports, were identified. After removing duplicates, 279 papers were screened, and from those, 258 were excluded. Overall, 21 publications were screened for eligibility, with 9 included in the qualitative synthesis (Figure 1).

A consensus was reached after the discussion of the proper method used to compare findings. For this purpose, the guidelines were group stratified by the type of procedure: treatment process, pharmacotherapy, management, and screening. Recommendations targeted at NCDs in children and adolescents (<18 years), pregnant women, other ethnic groups, therapeutic strategies, and secondary



Figure 1. Systematic reviews and meta-analyses (PRISMA) flowchart of the study selection process.

prevention for associated comorbidities were excluded from the systematic review.

The study used administratively collected secondary data and no ethics committee approval was required.

Results

The onset of HT in the European guidelines and the guidelines used in Southeast Asian countries was classified as BP \geq 140/90 mmHg. In the American guidelines, it was classified at lower levels (BP \geq 130/80 mmHg). The beginning of a patient's drug treatment in the first grade of HT was recommended mostly when lifestyle interventions had failed using combination therapy. American and European guidelines also strongly recommended that the start of medication should be based on the overall cardiovascular risk of the patient. Four guidelines advised to initiate hypertension treatment with one drug, but each guideline differed by the severity of hypertension. Recommendations on systolic blood pressure targets and blood pressure (BP) monitoring differed in these guidelines, as a few of them used age stratification or severity of HT as target criteria. The measurement of BP was recommended from 1 month to 5 years, depending on the guideline and patient's condition (Table 3).

Most guidelines recommended target HbA1c levels of <7%, but only a few altered these levels by the age of the patient (Guidelines 6 and 7). The recommended blood pressure target was estimated at <140/90 mmHg in Vietnamese and Indonesian guidelines, at <140/80 mmHg in European guidelines, and the estimation based on overall CVD risk was stated in the American and WHO guidelines (used in Myanmar). Metformin, if not contraindicated, was recommended as the first choice of treatment in all guidelines. If Metformin was not tolerated, Sulfonylurea was specifically recommended only in two guidelines. Six out of the seven guidelines recommended statin therapy to reduce CV risk (Table 4).

Although retinopathy, neuropathy, and increased albuminuria and eGFR levels have been identified as diabetesspecific risk enhancers that are independent of other risk factors in T2DM, in most guidelines, the frequency of examinations for these risk enhancers was not specified (Table 5).

Discussion

The use of systematic reviews for clinical practice guidelines is essential to classify, analyze, and summarize evidencebased guidance on certain topics. Conducting systematic reviews has been proven to be beneficial in various clinical areas, ranging from preclinical testing,²⁵ single diseases,²⁶ and risk factors,²⁷ to complex non-communicable diseases.²⁸ In our systematic review, aimed at describing and comparing guideline recommendations on HT and T2DM, we emphasized targeted patients' BP and HbA1c levels, patterns of drug treatment and management, and the screening of these diseases.

Selected American guidelines classified onset of HT as $BP \ge 130/80 \text{ mmHg}$, and to initiate a patient's drug treatment, guidelines first recommended the assessment of the patient's overall ASCVD risk. Guidelines used in IVM and Europe identified HT at a higher BP in comparison $(\geq 140/90 \text{ mmHg})$, but IVM guidelines recommended initiating drug treatment only when lifestyle interventions had failed. Only four guidelines differentiated their recommendations on the number of drugs used to initiate treatment by a patient's degree of HT (17, 18, 23, and 24), and the pill therapy to treat HT (single-pill combination therapy) was not specified in four guidelines (16, 18, 19, and 24). Systolic BP targets were differentiated by age in only two guidelines, with higher levels for older people, and the lowest recommended diastolic BP levels were 70 mmHg. Out of the seven guidelines, four guidelines recommended BP measurements/monitoring every few months, and recommendations in three guidelines were based on a patient's current BP levels.

All five guidelines recommended target HbA1c levels below 7%-6.5%, but only IVM guidelines included the reexamination of these levels every 3-6 months. Two guidelines had differentiated these levels by age groups. Metformin was recommended as the first choice of medical treatment, if not contraindicated, in all guidelines; however, if metformin was not tolerated, Sulfonylurea was specifically recommended as the first choice of medical treatment by only two guidelines (20 and 22). Statin therapy, to reduce CVD risk, was recommended in all guidelines except 1 (22), and blood glucose self-monitoring was recommended only in two guidelines. Screening recommendations varied remarkably among the guidelines, most recommending annual kidney disease screenings (four guidelines) and annual foot examinations (three guidelines). Patient prevention against certain communicable diseases was recommended only in two guidelines.

Among the recommendations, there were no major differences between the guidelines with regards to the Class of recommendation and Level of evidence (among the ones which included such grading). The absence of essential quality rating systems in guidelines implies the necessity of their improvement to support evidence-informed decision-making in healthcare provision.²⁹ The systematic review-Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach to develop a common and transparent system for grading the quality of evidence and the strength of recommendations³⁰—should be used in referral guidelines for all basic services.³¹ As derivation from existing guidelines and adaptation to local context may lack transparency, it is crucial to set a working group with expertise in medical content and methods, but also in the values and preferences of

Table 3. Comparise	on of guidelines recor	mmendations—hyperten	sion.				
Recommendation	_	2	3	4	5	8	6
	Arnett et al. ¹⁶	Williams et al. ¹⁷	Whelton et al. ¹⁸	Perk et al. ¹⁹	World Health Organization ²⁰	Indonesian Society of Hypertension ²³	Vietnam Ministry of Health ²⁴
Diagnosis of hypertension	≥I 30/80 mmHg	≥I40/90 mmHg	≥I30/80mmHg	≥I 40/90 mmHg	≥I 40/90 mmHg	≥I 40/90 mmHg	≥I40/90 mmHg
Start medication in grade/stage I hypertension when;	Estimated 10-year ASCVD risk ≥10%	Lifestyle interventions have failed or at high CV risk or with HMOD	Estimated 10-year ASCVD risk <10% and an SBP ≥140 mmHg or a DBP ≥90 mmHg	High or very high CVD risk	Lifestyle interventions have failed	Lifestyle interventions have failed	Lifestyle interventions have failed
	I; SBP: A; DBP: C-EO	l; A	I, G-LD	I; C (Strong)	NA	NA	NA
Number of drugs used to initiate treatment	Based on overall ASCVD risk assessment	HT degree I or >80years: I drug Other: 2-3 drugs	HT degree I and BP goal < I 30/80mmHg: I drug HT degree 2 + average BP more than 20/10mmHg above their BP target: 2 drugs	No recommendation	One	HT degree I or >80years: I drug Other: 2–3 drugs	HT degree I: one drug HT degree 2–3: two or more drugs
	NA	NA	C-EO	I	NA	NA	NA
Single pill combination	No recommendation	Initial therapy	No recommendation	No	If BP still \geq I40 or \geq 90	Initial therapy	No recommendation
tnerapy				recommendation			
	I	l; A	I	NA	NA	1	NA
SBP target for age groups DBP target	Based on overall ASCVD risk assessment	120−129mmHg (<65years) 130− 139mmHg (≥65years and >80years) <80mmHg but not <70mmHg	130/80 mm Hg	140/90 mmHg	No recommendation		No recommendation
	NA	l; A l; A l; C	I; SBP: B-R DBP: C-EO	II; A (Strong)	NA	NA	I
BP measurements/ monitoring	Every 3-6 months	<120/80 mmHg—every 5 years 120–129/80– 84 mmHg—every 3 years 130–139/85–89 mmHg— yearly ≥ 140/90 mmHg 5 tage 1—monthly Stage 2 and higher—weekly	HT stage 1: Every 3–6 months, if ASCVD risk >10% then every month HT stage 2: every month Normal BP: once a year	Several months ^a	Every month until improvement/ stabilization of BP	< 20(80 mmHg-every) 5 years $ 20- 29(80-84 \text{ mmHg}\text{-every})$ 3 years $ 30- 39(85-89 \text{ mmHg}\text{-})$ yearly $\geq 40(90 \text{ mmHg}\text{-})$ yearly $\geq 40(9$	 < 130/<85 mm Hg— annually 130–139/85– 89 mmHg—every 3 months 140–159/90–99 mmHg— weekly 160–179/100– 160–179/100– 100 mmHg—daily > 180/110 mmHg—daily
	NA	NA	I, B-R	NA	NA	NA	NA

ASCVD: atherosclerotic cardiovascular disease; DBP: diastolic blood pressure; HMOD: hypertension-mediated organ damage; SBP: systolic blood pressure; ^ameasurements should be made over a period of several months to achieve an acceptable definition of an individual's "usual" BP and to decide about initiating drug treatment.

Recommendation	1	4	5	6	7
	Arnett et al. ¹⁶	Perk et al. ¹⁹	World Health Organization ²⁰	Soelistijo et al. ²¹	Vietnam Ministry of Health ²²
Target HbA1c level	Recommended <6.5%	Recommended <7%; <6.5% may be useful	Recommended <7%	Recommended <7%	Recommended <7% but with other variables
Different HbA1c targets for elderly	No recommendation	No recommendation	No recommendation	Recommended between 7.5–8.5%	Recommended <8%
	-	-	-	В	NA
Blood pressure target	Based on CVD risk	<140/80 mmHg	Based on CVD risk	<140/90 mmHg	<140/90 mmHg
	I; SBP: B-R DBP: C-EO	l; A (Strong)	NA	В	NA
Examination of patient's HbA1c levels	No recommendation	No recommendation	Recommended	Recommended every 3 months	Recommended at least 2× year
each 3–6 months	_	_	NA	E	NA
Metformin as the	Recommended	Recommended	Recommended	Recommended	Recommended
first choice if not contraindicated	IIa; B-R	IIa; B (Strong)	NA	NA	NA
Sulfonylurea as	No recommendation	No recommendation	Recommended	No recommendation	Recommended
the first choice if metformin not tolerated	-	-	NA	-	NA
Statin therapy to	Recommended	Recommended	Recommended	Recommended	No recommendation
reduce CV risk	I; A	I; A (Strong)	NA	С	-
Blood glucose self- monitor	No recommendation	No recommendation	No recommendation	Recommended	Recommended
	_	-	-	В	-

 Table 4. Comparison of treatment process and pharmacotherapy—type 2 diabetes mellitus.

CVD: cardiovascular disease; HbA1c: glycated hemoglobin.

Table 5. Comparison of management and screening—type 2 diabetes mellitus.

Recommendation	I	4	5	6	7
	Arnett et al. ¹⁶	Perk et al. ¹⁹	World Health Organization ²⁰	Soelistijo et al. ²¹	Vietnam Ministry of Health ²²
Retinal disease screening	Diabetes-Specific Risk Enhancer—frequency not specified	No recommendation	Recommended every 2 years	Recommended	Recommended
	NA	-	NA	В	NA
Psychological distress screening	Recommended	No recommendation	No recommendation	Missing standard	Recommended but not specified
	Consideration ^a	-	-	NA	NA
Kidney disease annual screening	Recommended but frequency not stated	No recommendation	Recommended	Albuminuria examination recommended annually	eGFR and albuminuria examination recommended
	NA	_	NA	В	NA
Annual foot	No recommendation	No recommendation	Every 3–6 months	Recommended	Recommended
examination	-	-	NA	NA	NA
Patient prevention	No recommendation	No recommendation	No recommendation	Recommended	Recommended
	_	_	_	NA	NA

CVD: cardiovascular disease; eGFR: estimated glomerular filtration rate; HbA1c: glycated hemoglobin. ^aExample considerations for addressing social determinants of health to help prevent ASCVD events.

communities.³² Adjustments and implementations of guidelines, on a national level, can be feasibly achieved through proceeding within methodological standards, feasible frameworks, and guides such as the GRADE Handbook.^{30,33,34} Pragmatic approaches are required in settings where resources are limited; thus, purposeful clinicians' workgroups are needed to make sustained efforts for guideline improvement.^{35,36}

As stated, the systematic review was conducted in order to propose amendments to currently used clinical practice guidelines concerning overall management of HT and T2DM in Indonesia, Vietnam, and Myanmar based on the findings; however, the possibility of their implementation is severely limited. The current situation in Myanmar precludes the implementation of the review's findings, as the military seized power in February 2021. The country is in an unstable political environment, and the military is attempting to maintain power by shutting down all communication, whether via the internet or mobile data. Both Indonesia and Vietnam have centralized authority, which means that the government has a greater proportion of decision-making power. As a result, any modification or usage of the guidelines is strictly monitored by this authority.

Promoting and assisting the modification and implementation of these guidelines remains one of the primary goals of the SUNI-SEA project; therefore, the project team is considering a new policy with this purpose in view. Furthermore, project activities include developing a strategy for measuring the use of existing guidelines in primary practice in Vietnam.

Limitations

Although we proceeded in our systematic review according to the PRISMA statement, we were unable to uphold all items in the PRISMA checklist. Due to the heterogeneity among the American, European, and IVM guidelines, we could not properly assess the risk of bias within or across the recommendations. Five out of nine guidelines did not include the Class of recommendations, and four out of nine guidelines did not include the Level of evidence. Moreover, some of the selected recommendations were identified in the text of a guideline but these recommendations were only supported by additional studies.

Some identified guidelines in a few sections referred to additional guidelines, which were not included in this review. This content could include additional recommendations not stated in a selected guideline resulting in a biased not-applicable (NA) for certain recommendations.

As the guidelines are often robust and comprehensive in their topics, we were forced to exclude many further complications and comorbidities of HT and T2DM to retain the aimed intention of this review. We observed significant differences among guidelines being used in countries of Southeast Asia and those from Europe and the USA. Most of those evaluated did not mention important attributes, such as the Class of recommendation or the Level of evidence. Without those, the use of recommendations is feasible, but users might be less willing to use them for clinical decisions in their clinical practice. It is recommended that these guidelines are revised and completed to be used as credible sources in the manner of evidence-based medicine.

Author contributions

MR, JM, and PS conceptualization; JM and PS, manuscript writing and analysis; JM, PS, and PPT, methodology; RM, PPT, and MM, review and editing. All authors contributed significantly to the study and read and approved the final manuscript version.

Declaration of conflicting interests

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Significance for public health

To support the adaptation of clinical practice guidelines in Southeast Asian countries, this systematic review offers a highquality, thorough summary of recommendations on the management of hypertension and type 2 diabetes mellitus disease. The revision and completion of those guidelines are essential for improving their quality and usage, as it was discovered during the review that the majority of the evaluated guidelines omitted key elements like the Class of recommendation or the Level of evidence. By including these attributes, they will become a reliable source in the area of evidence-based medicine.

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Availability of data and materials

The database used during the current study are available upon reasonable request from the corresponding author.

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