Evidence-based Diabetes Care in Indonesia - Knowledge translation and transfer of best practice

Evidence-based diabeteszorg in Indonesië - vertaling en toepassing van kennis in de gezondheidszorg
(met een samenvatting in het Nederlands)

Tata laksana diabetes di Indonesia – translasi bukti ilmiah dan transfer praktik terbaik
(dengan ringkasan dalam Bahasa Indonesia)

Proefschrift

ter verkrijging van de graad van doctor aan de Universiteit Utrecht op gezag van de rector magnificus, prof.dr. G.J. van der Zwaan, ingevolge het besluit van het college voor promoties in het openbaar te verdedigen op dinsdag 27 september 2016 des middags te 12.45 uur

door

Indah Suci Widyahening

geboren op 11 oktober 1973
te Jakarta, Indonesië

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The Solace

"Have We not expanded for you your chest?"
"And We removed from you your burden,"
"Which weighed down your back?"
"And We exalted for you your reputation?"
"For indeed, with hardship (will be) ease:"
"Indeed, with hardship (will be) ease,"
"So when you have finished (your duties), then stand up, (for worship),"
"And to your Lord direct (all) your longing."

Sura 94 of the Holy Quran

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Contents

Chapter 1 General Introduction

Worldwide the prevalence of diabetes has been growing over the last decades, and is now considered one of the greatest epidemics in the world. The burden of diabetes is higher in the developing countries especially those in the Asia Pacific region. Indonesia is the fourth most populated country in the world with approximately 250 million people and consequently, although the prevalence of diabetes is relatively low (6.9% in 2013), Indonesia is continuously among the top ten countries worldwide in the number of people living with diabetes.[1] More than 70% of people with diabetes in Indonesia remain un-diagnosed[2] and among those diagnosed and receiving treatment, more than 60% do not achieve blood glucose control.[3]

Evidence-based Practice (EBP) aims to provide clinicians and patients with choices on the most effective care based on the best available research evidence.[4] Clinical practice guidelines (CPG) increasingly are becoming a familiar part of the health care practice in Indonesia. High-quality clinical practice guidelines can improve the quality of decisions and care. The implementation of clinical practice guidelines for the management of diabetes has beneficial effects for the individual with diabetes, including a significant reduction in complications associated with diabetes as well as hospitalization.[5, 6] Clinical practice guidelines have also been shown as a pragmatic approach to improve the quality of care on the national level.[7] In 1993, the first guideline concerning diabetes was published in Indonesia. This was a consensus-based guideline with evidence derived and adapted from existing international guidelines on diabetes. The consensus mainly concerns guidance on both the prevention and the treatment of diabetes.

The concept of Evidence-based Practice (EBP) was introduced to the health professions of Indonesia in early 2000[8] and to date the interest is still growing. However, globally current interest has been shifting towards the strategy to enhance the use of evidence in practice that is also known as “knowledge translation”.

Knowledge translation is defined as "a dynamic and iterative process that includes the synthesis, dissemination, exchange and ethically sound application of knowledge to improve health, provide more effective health services and products and strengthen the healthcare system".[9] Although lack of application of findings from research to improve health is a global problem, it is of particular concern in developing countries where limited resources cannot be wasted on health care interventions that do not work or may even cause additional harm.[10]

The overall aim of this thesis is to explore the status of knowledge translation on diabetes care in Indonesia. The specific questions to be answered are,

1. How is the best evidence from research concerning the management of diabetes in Indonesia established?
2. How is the utilization of clinical practice guidelines as a third generation knowledge base on diabetes in Indonesia?
3. Can teaching activities on Evidence-based Practice that are already implemented in developed countries be adapted and then adopted in the developing countries setting?

Outline of this thesis

In **chapter 2,** we describe the prevalence of diabetes in the Asian countries and the high burden in both the developed and less developed countries. One type of evidence source which has considerable potential to improve the quality and the outcome of health care is the evidence-based clinical practice guidelines. **Chapter 3** describes the implementation of Evidence-based Practice in Indonesia by studying the utilization of a type 2 diabetes clinical practice guideline among primary care practitioners in Indonesia while the development of a clinical practice guideline in Indonesia is illustrated in **chapter 4**. Published clinical evidence is one component

of Evidence-based Practice and in **chapter 5,** we examined the quality of published clinical evidence by Indonesian researchers. Chapters 6 and 7 focus on the effort to provide a learning activity on Evidence-based Practice for undergraduate medical students in Indonesia and Malaysia; **chapter 6** describes the development process of an Evidence-based Practice teaching module through adaptation of an existing one, while **chapter 7** reports the assessment and comparison of the outcomes of students participating in the Evidence-based Practice module in the three universities (University Medical Center Utrecht, Universitas Indonesia and University of Malaya). In **chapter 8,** the relevance of Evidence-based Practice in Indonesia and the need to move from Evidence-based Practice to knowledge translation in diabetes care is discussed.

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Chapter 2

Variation in diabetes prevalence in Asian countries and its relation to the country characteristics

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(manuscript in-preparation)

Abstract

Background *- To explore the variation in diabetes prevalence across Asian countries and determine the extent of the variation may be explained by differences in country's health system quality and socioeconomic determinants.*

Methods *- An ecological analysis which utilizes publicly available data from World Health Organization (WHO), World Bank (WB), and International Diabetes Federation (IDF). Aggregate data at country level on the determinants (ratio of physicians per 1000 population, mean diabetes related expenditures, quality of health governance, number of motor vehicles per 1000 population, prevalence of hypertension, and obesity) and outcome (diabetes prevalence) were extracted from each respective databases for all the 36 Asian countries. Geographical variation in diabetes prevalence across Asian countries was examined by differentiating common cause variation from special cause variation graphically using control charts. Associations between country-level determinants and diabetes prevalence were examined using linear regression analysis.*

Results *- The control chart shows special-cause variation in diabetes prevalence in 58% of the Asian countries; nine countries were below the 99.8 percent control limits while twelve were above it. Fifteen (42%) Asian countries suggest common-cause variation. Three country characteristics independently associated with diabetes prevalence were hypertension prevalence (β 0.39, 95% CI 0.22 to 0.55; p-value < 0.001), obesity prevalence (β 0.15, 95% CI 0.13 to 0.18; p-value < 0.001), and quality of health care governance (β 0.18, 95% CI 0.04 to 0.34; p-value=0.02).*

Conclusions *- There is a considerable geographical variation in diabetes prevalence across Asian countries. A substantial part of this variation could be explained by the differences in quality of health care governance, hypertension prevalence and obesity prevalence. Further study is needed to identify good practice related to diabetes that are particular to the specific sub-regions in Asia, in order to promote effective public health intervention in the prevention of diabetes.*

Introduction

The increasing number of people with diabetes worldwide, and the grim consequences of the disease with close to five million deaths each year, constitutes one of the largest epidemics in human history.[1] Without effective prevention and management programs the burden will continue to increase globally. Type 2 diabetes makes up about 85% to 95% of all cases of diabetes in high-income countries and may even account for a higher percentage in low- and middle-income countries.[2] The International Diabetes Federation (IDF) reported that 382 million people have diabetes worldwide and more than half of them live in Asia.[3]

Six of the ten top countries with the highest numbers of diabetic patients were Asian countries and by 2030, World Health Organization (WHO) has predicted that seven Asian countries will be among the top ten countries with the highest diabetes prevalence.[4] The ranking likely results from a combination of large populations in the Asian region with rapidly rising prevalence rates of type 2 diabetes and its risk factors.[5]

The differences in prevalence of diabetes across Asian countries have not been well addressed. Addressing the gap may help improving public health efforts in stalling the disease progress. According to Deming, differences could be attributed to variation in the process. Deming differentiated variation into common cause variation (i.e. variation that is within what is expected) and special cause variation (i.e. variation that is outside what is expected).[6, 7]

The health system plays a key role in the process of controlling and managing diabetes, thus it might have a role as the cause of variation. Further research is clearly needed to understand whether country's health system influences the diabetes epidemic in Asia. WHO describes health systems in six core components or "building blocks": (i) service delivery, (ii) health workforce, (iii) health information systems, (iv) access to essential medicines, (v)

financing, and (vi) leadership/governance.[8] Thus, this study aims to explore the variation in diabetes prevalence across 36 Asian countries and determines to what extent variation may be explained by differences in the health system components and the existence of known risk factors of non-communicable diseases (NCDs) such as affluent life-style, hypertension and obesity.

Methods

Study design and data collection

This study is an ecological study which utilizes publicly available data and reports by the World Health Organization (WHO)[9], the International Diabetes Federation (IDF)[3] and the World Bank[10].Aggregate data at country level on the determinants and the outcome were extracted from each of the 36 Asian countries. The determinants were the potential risk factors for diabetes (affluent lifestyle, hypertension and obesity prevalence) and components of the WHO's building blocks of the health system which is publicly available; consisted of health human resource, health care financing and quality of health care governance.[8, 11]

Health human resource is represented by the ratio of physicians in 1000 population.[9] Health care financing is measured by the mean diabetes related expenditures per person per year in US$.[12] Leadership and governance in health was measured using the Worldwide Governance Indicators (WGI) which is a research dataset by the World Bank built on a survey on the experts' views in political stability, government effectiveness, voice and accountability, rule of law, regulatory quality, political stability and control of corruption of one country. The experts came from various enterprises, regular citizen and experts in industrial and developing countries. These data were gathered from a number of survey of households and firms, commercial business information providers, non-governmental organizations, and

public sector organizations. The data is currently used by the World Bank and several other donor agencies to measure the quality of governance of a country.[13] Each of the six parameters in the survey was ranked from -2.5 to +2.5. The ranks were sum up as the total score for the quality of healthcare governance of a country, which ranges from -15 (worst) to +15 (best).[14]
In addition, we also consider other factors for each country, such as number of motor vehicles (per 1000 population) which represents affluent lifestyle, prevalence of hypertension above 18 years of age (defined as Systolic Blood Pressure>=140 OR Diastolic Blood Pressure>=90 mmHg; age-standardized estimate) and prevalence of obesity above 18 years of age (Body Mass Index >= 25; age-standardized estimate).

As the outcome of interest in this study, we took country's diabetes prevalence above 18 years of age which was defined as fasting blood glucose >=7.0 mmol/L or on medication (age-standardized estimate).[9]

Statistical analysis

We determined the range, mean and standard deviation of diabetes prevalence and the potential determinants. The weighted average of diabetes prevalence was estimated using mixed model analysis.

A control chart is used to explore variation of diabetes prevalence across Asian countries by differentiating common cause variation from special cause variation graphically.[6, 7]The control chart was depicted by plotting weighted mean of diabetes prevalence on the y-axis against a measure of their precision, i.e. standard deviation on the x-axis. The chart consists of five horizontal lines, one central line with two lines below and above it. The central line represents the weighted mean of diabetes prevalence, while the other two lines above and below the central line indicate 95% limits (2 standard deviation) and 99.8% limits (3 standard deviation) of the weighted mean of diabetes prevalence. We use three standard deviations as

the control limits. Countries with a diabetes prevalence within the control limits (3 standard deviation) are regarded to show common-cause variation while those outside the control limits are considered to show special-cause variation.

Unadjusted associations between diabetes prevalence and country-level determinants were examined using bar chart. The pooled country-level of number of physicians per 1000 people, mean diabetes related health expenditure, quality of healthcare governance, number of motor vehicles per 1000 people, hypertension prevalence and obesity prevalence were plotted using multiple double-bar charts against the average diabetes prevalence of countries located below, within and above the control limits in the control chart.

The relationships between country-level determinants and diabetes prevalence were examined using linear regression analysis. Two-tailed Wald test at significance level of alpha equal to 5% was used to determine the statistical significance of the association. Stata statistical package version 12 was used to perform statistical analysis.[15]

Ethical approval

No ethical approval is required for analysis of publicly available data,

Results

We observed that diabetes prevalence varied across Asia, starts from 5.6% in North Korea to 23% in Qatar, with the mean (SD) prevalence of 11.60 (4.25) %. The 36 Asian countries showed marked variation in all determinants as shown in Table 1. The ratio of physicians per 1000 population ranged between 0.07 in Timor Leste to 7.74 in Qatar. The average diabetes related expenditure per person was 804 dollars, ranged from 31 to 4308 dollars. Ten countries (Japan, Singapore, Qatar, South Korea, United Arab Emirates,

Kuwait, Brunei Darussalam, Oman, Saudi Arabia and Bahrain) spent more than 1000 US$ on diabetes health related care per person per year while seven other countries (Myanmar, Bangladesh, Pakistan, Nepal, Lao, Cambodia and India) spend less than 100 US$. The average quality of health care governance was generally low with the mean score of -2.26 an only nine countries (Singapore, Japan, South Korea, Qatar, Brunei Darussalam, United Arab Emirates, Malaysia, Oman, and Bhutan) had a positive score indicating good quality health care governance. The average number of motor vehicles per 1000 population was 180; ranged from 3 in Bangladesh to 588 motor vehicles per 100 population in Japan.

Table 1. Characteristic of the Asian countries (n=36)

Country characteristics	Mean (SD)	Range
Diabetes prevalence (Fasting blood glucose >=7.0 mmol/L or on medication; age-standardized estimate)	11.60 (4.25)	5.6; 23.0
Number of physicians (per 1000 population)	1.45 (1.44)	0.07; 7.74
Mean diabetes related health expenditure per person (USD)*	804 (1065)	31; 4308
Quality of healthcare governance	-2.26 (4.76)	-9.53; 9.45
Number of motor vehicles (per 1000 population)*	180 (194)	3; 588
Raised blood pressure prevalence (SBP>=140 OR DBP>=90; age-standardized estimate)	23.82 (4.24)	10.80; 31.40
Obesity prevalence (BMI >= 25; age-standardized estimate)	39.6 (21.3)	14.5; 78.1

* no data available for North Korea

Special- and common-cause variations in diabetes prevalence

Figure 1 shows the results of the control chart that explored variation in diabetes prevalence across 36 Asian countries. The weighted mean of diabetes prevalence was 10.5 (99.8% CI 8.8; 12.2). Diabetes prevalence in fifteen (42%) Asian countries laid within the 99.8 percent control limits which suggests common-cause variation. Diabetes prevalence in nine (25%) Asian countries were below the control limits while twelve (33%) Asian

countries diabetes prevalence were over it. Thus, special-cause variation appeared present for twenty-one (58%) Asian countries.

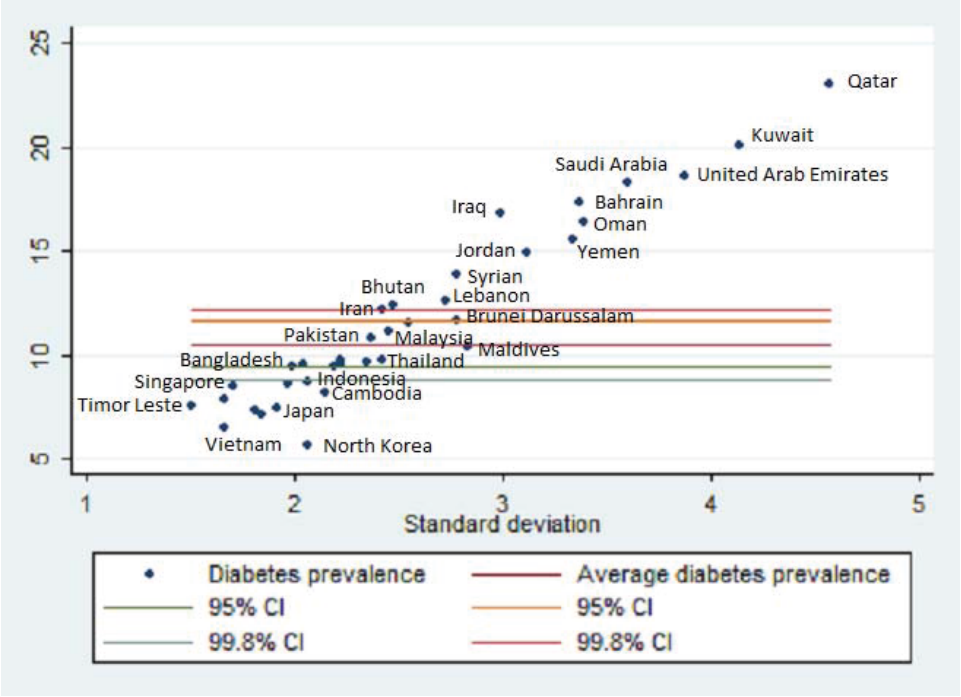

Figure 1. Control chart of diabetes prevalence across Asian countries.

Geographical variations in diabetes prevalence

Figure 2 shows the map variation of diabetes prevalence across Asian countries. We observed that countries located above control limit in the control chart (diabetes prevalence > 12.2%) are mostly located at the Western part of the continent (the Middle East region) while countries below the control limit (diabetes prevalence <8.8%) like North Korea, Vietnam, Myanmar, Philippines, Timor Leste and Japan are located at the eastern part of the continent.

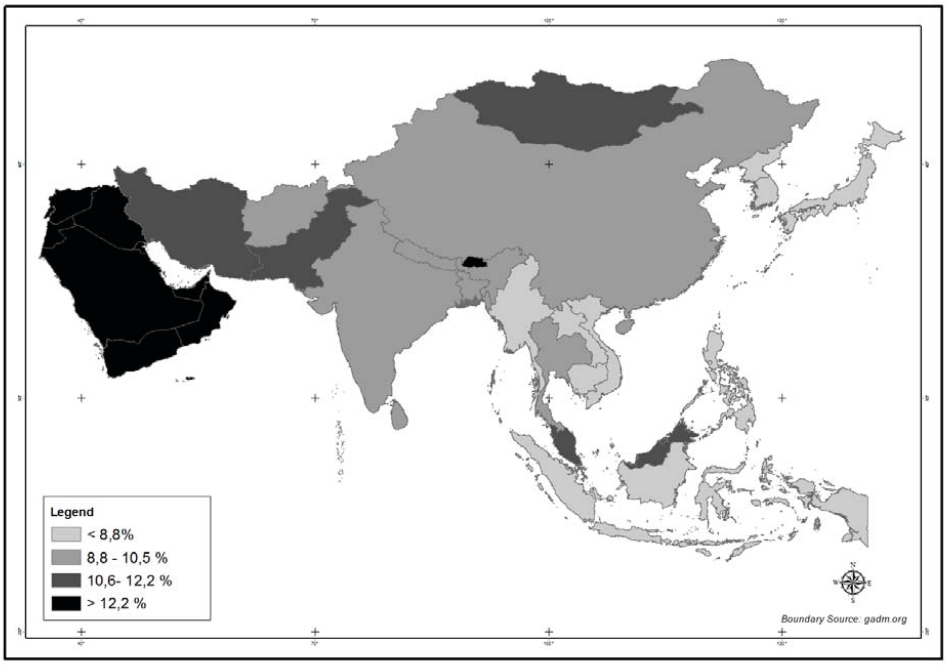

Figure 2. Map of Asian countries for diabetes prevalence

Associations between country-level characteristic and diabetes prevalence

Unadjusted associations - The relationships between country-level determinants and diabetes prevalence are shown in figure 3 using multiple double-bar charts. The charts show that diabetes prevalence increased in the same direction as the prevalence of hypertension or obesity. The number of physicians, mean diabetes related expenditure per person, quality of healthcare governance, and number of motor vehicles were not associated with diabetes prevalence.

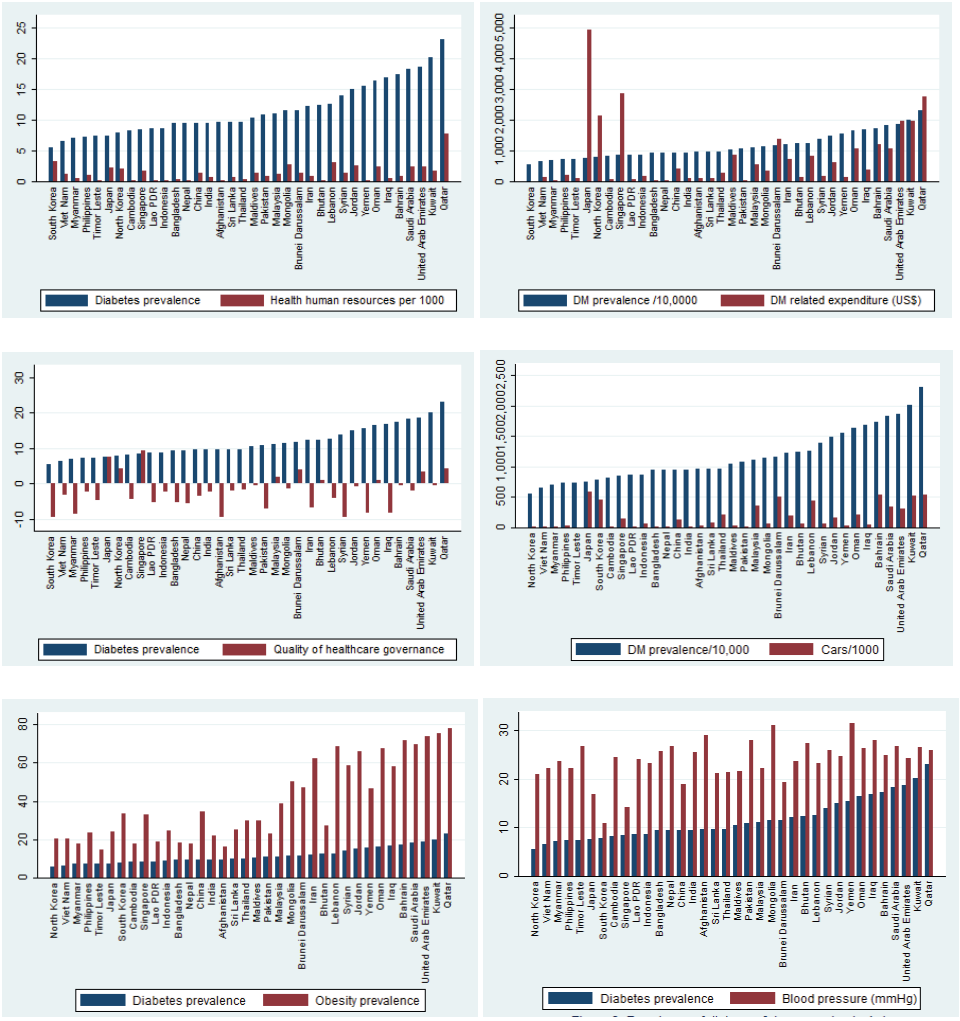

Figure 3. Relationship between country level characteristics and diabetes prevalence in Asia

The comparison of characteristics of the countries with the average diabetes prevalence below, within and above the control limits (≈ 3 standard deviation) showed that diabetes prevalence had positive linear relationships with country's hypertension and obesity prevalence (figure 4).

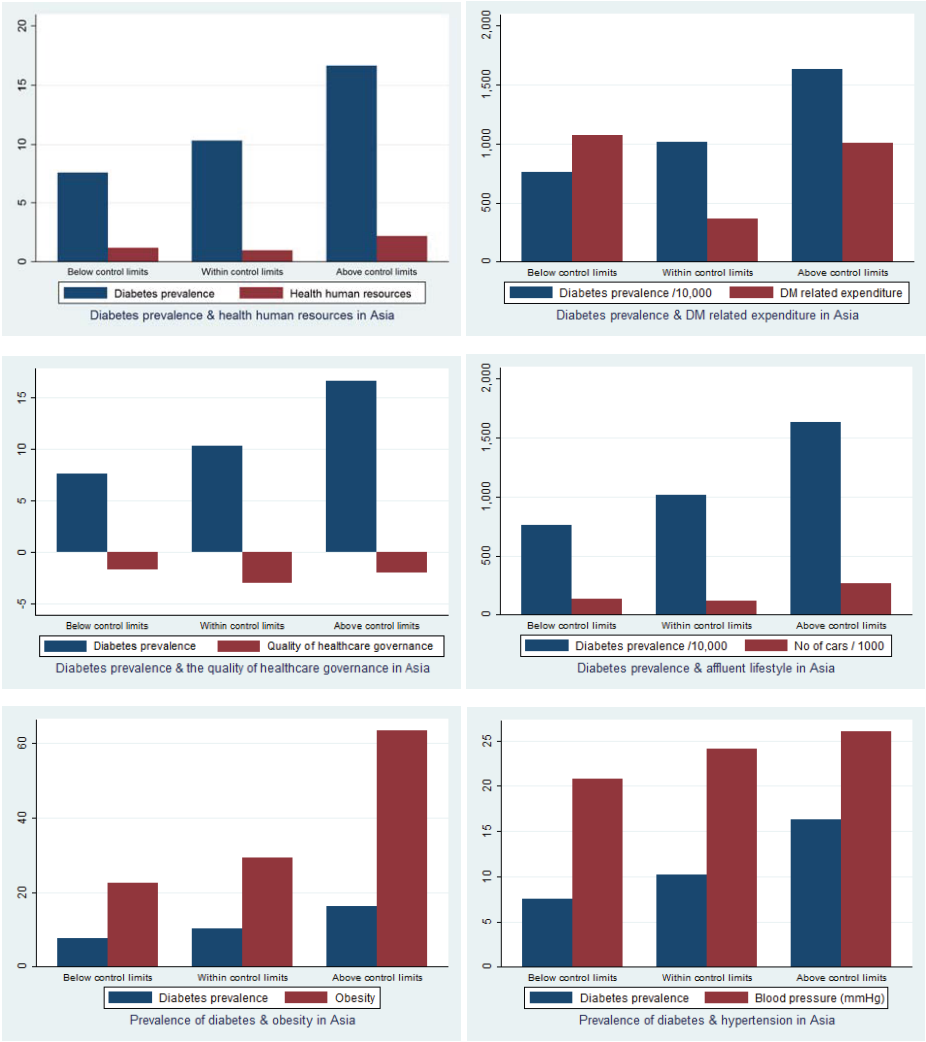

Figure 4. Relationships between country level characteristics and grouped diabetes prevalence (i.e below control limit, within control limit and above control limit).

Adjusted associations - The results of the multivariable linear regression analysis to examine the association between country characteristic and diabetes prevalence are shown in Table 2. In the model, three determinants have a significant independent association with diabetes prevalence. First, hypertension, as the strongest factor associated with diabetes prevalence. In every percent of hypertension prevalence, diabetes prevalence increased by 0.39 percent (95% CI 0.23 to 0.55; p<0.001). Second, the obesity prevalence. For every percent increase in obesity prevalence, diabetes prevalence increased by 0.15 percent (95% CI 0.13 to 0.18; p<0.001). Third, quality of health care governance. For every unit increase in the country's quality of healthcare governance, diabetes prevalence increased by 0.18 percent (95% CI 0.04 to 0.32; p = 0.02). The R-squared of this model is 0.88, meaning approximately 88% of the variability of diabetes prevalence is accounted for the variables in the model.

Table 2. Associations between determinants and diabetes prevalence across Asian countries (n=36)

Country characteristics	**Univariable model β (95% CI)**	**Multivariable model β (95% CI)**
Number of physicians (in 1000 population)	1.43 (0.53-2.33)	###
Mean diabetes related health expenditure per person (USD)*	0.001 (-0.0003; 0.002)	###
Quality of healthcare governance	0.15 (-0.16; 0.46)	0.18 (0.04; 0.33)**
Motor vehicles (in 1000 population)	0.01 (0.004; 0.02)	###
Hypertension prevalence (SBP>=140 OR DBP>=90; age-standardized estimate)	0.43 (0.11; 0.74)	0.39 (0.23; 0.55)**
Obesity prevalence (BMI >= 25; age-standardized estimate)	0.18 (0.15; 0.21)	0.15 (0.13; 0.18)**

R^2= 0.88 ### Variables omitted in the final multivariable model based on adjusted R-squared

**p<0.05

Discussion

Our study shows two major findings. First, there is a considerable geographical variation in diabetes prevalence across 36 Asian countries. Second, differences in the quality of health care governance, hypertension prevalence and obesity prevalence across these countries contributes to this major variation observed.

We observed that countries with the highest diabetes prevalence in Asia are located at the western part of the continent (the Middle East region) while countries which have the lowest diabetes prevalence are located at the eastern part of the continent.

In our study, we found that obesity and hypertension prevalence are strongly correlated with the diabetes prevalence. The global rise in diabetes prevalence is largely driven by modifiable risk factors – particularly physical activity, overweight, and obesity. Across Asian countries, the prevalence of obesity is also highest in the Eastern Mediterranean region and lowest in the South-East Asia and Western Pacific region.[16] Our finding indicates that there might be favorable practices conducted in the eastern part of Asia that has succeeded in stalling the prevalence of diabetes. Several ecological analyses and systematic reviews reported that sedentary life-style and westernized diet,[17] fish and seafood consumption[18], urban exposure,[19, 20] and over-dependence on motorized transportation[21] may contribute to the global rise in obesity and diabetes prevalence.

Several large population-based cohort studies confirmed that high normal blood pressure as well as established hypertension was strongly and independently related to the development of type 2 diabetes.[22-26] Possible underlying mechanisms include, the occurrence of endothelial dysfunction which is associated with both elevated blood pressure and insulin resistance which lead to the development of type 2 diabetes, and the elevation of

inflammatory markers at the increased of the blood pressure which could also enhance the development of type 2 diabetes.[22] Other mechanism such as the use of certain blood pressure lowering drugs was also suspected to be related to the development of type 2 diabetes.[27]

With the 4.1 billion people resides in Asia, a single percent increase of hypertension or obesity prevalence may increase the number of people with diabetes in the region by 16 or 6.1 million respectively.

In our study, better governance in health care system was associated with an increased prevalence in diabetes. Strong health governance at all levels is necessary to ensure that health care resources achieve affordable, accessible quality health care for all.[8] Typically, when health care governance is carried out efficiently, effectively, and equitably, health care system is expected to improve health outcomes i.e. lower prevalence of diseases. However, in the case of chronic diseases such diabetes, good quality of the health system may lead to earlier and higher detection of diabetic patients that will increase the country's prevalence of diabetes and the improved survival rates of people with diabetes by improving the management of diabetes. Subsequent studies need to further examine this association critically.

It should be realized that much of the data utilized in this study including diabetes prevalence data were derived from estimates. For countries without available local data, estimates are based on modeling using pooled estimates from countries that considered as similar in geography, ethnicity, and economic development.[16] Furthermore, numerous available country data are not necessarily equivalent due to methodological differences. Other limitation is publication bias. Using an open data source may resulted in missing data on certain potentially important components of health systems such as health care delivery, information system, and availability of medical products and technologies. However, the determinants we have chosen in this study was also

used by many stakeholders as their indicators in analyzing socio-economic status of a country, thus our results has presented the best available current evidence on diabetes status of Asian countries.

Conclusion

This study shows considerable geographical variation in diabetes prevalence across Asian countries. Countries with the highest diabetes prevalence in Asia are located at the western part of the continent (the Middle East region) while countries which have the lowest diabetes prevalence are located at the eastern part of the continent. A substantial part of this variation could be explained by the differences in quality of health care governance, hypertension prevalence and obesity prevalence. Further study is needed to identify special practice or process related to diabetes that are particular to these regions in Asia, in order to promote effective public health intervention in the prevention of diabetes.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

Indah S. Widyahening (ISW), Gbenga A. Kayode (GAK), and Diederick E. Grobbee (DEG) conceptualized and designed the study. ISW and Grace Wangge (GW) carried out the literature review, data extraction, result interpretation and drafted the manuscript while GAK did the data analysis. All of the authors reviewed and approved the final version of the manuscript.

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Chapter 3

Awareness, agreement, adoption and adherence to type 2 diabetes mellitus guidelines: a survey of Indonesian primary care physicians

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Abstract

Background - *To assess the degree of awareness, agreement, adoption and adherence of physicians in Indonesia to type 2 diabetes mellitus guidelines, and their association with characteristics of the responders.*

Methods - *Questionnaire survey among General Practitioners (GPs) attending the Indonesian Association of Family Practitioners annual conference in November 2012. The proportion of GPs who were aware of, agreed with, adopted, and adhered to the seven recommendations in the guidelines (screening for diabetes, diagnosis, lifestyle modification, use of sulfonylurea, target blood glucose, target blood pressure, and use of statin) were calculated in the total number of responders.*

Results - *Of the 399 GPs participating, 383 (89%) were aware of the existence of Indonesian type 2 diabetes guidelines. Awareness for each recommendation varied from 66% to 91%. The recommendation to use a random blood glucose test for diagnosing patients with classic diabetes symptoms had the least awareness (265/399, 66%) and least agreement (163/399, 41%). The recommendation on statin use was the least adopted (192/399, 48%), while the least adherence (7/399, 2%) was found for the recommendation on screening for diabetes for patients with risk factors. Years of practice experience and proportion of diabetes patients seen in their practice were independently related with adherence to statin prescription.*

Conclusions - *High awareness of the Indonesian type 2 diabetes guideline does not necessary lead to adoption or adherence to recommendations important for outcomes and quality of care. The awareness-to-adherence model helps in identifying barriers for the use of guidelines.*

Background

A study by the World Health Organization (WHO) estimated that the total number of people with diabetes will increase from 171 million in 2000 to 366 million in 2030; mostly in developing countries [1]. This is due to population growth, aging, urbanization, and increasing prevalence of obesity and physical inactivity. The Basic Health Research Survey conducted by the Indonesian Ministry of Health in 2007 involved 24,417 participants living in urban area from all over Indonesia found that the prevalence of diabetes in Indonesia was about 6%, and about two thirds of that percentage are unaware that they have diabetes.[2] Therefore, Indonesia became the seventh largest country with diabetes people in the world.[3]

Diabetes mellitus is a complex chronic disease that requires lifelong self-management and continuous medical care to prevent its acute complications and reduce its associated chronic health risks.[4] Type 2 diabetes, which is resulted from a progressive insulin secretory defect on the background of insulin resistance has been recognized as an emerging health problem in Asia Pacific, including Indonesia. On the other hand type 1 diabetes, which is resulted from β-cell destruction is less common in the region.[2,4,5] However, the two decade existence of the Indonesian guidelines on diabetes management seems insufficient to achieve the targets in diabetes control. Currently, about 68% of type 2 diabetes patients being cared in secondary and tertiary hospitals in Indonesia have poor blood glucose control (HbA1c > 7% or >53 mmol/mol).[6]

Guidelines may assist patients and health professionals in achieving optimal management of diabetes. The Indonesian Society of Endocrinology (Perkeni) introduced a guideline on the management and prevention of type 2 diabetes mellitus in 1993, and revised it on regular basis since then.[7] This guideline provides selected recommendations that have been derived from

a selection of internationally established guidelines[4,8-10] and consensus of Indonesian experts in endocrinology.

Several surveys have shown that the adherence varies per guideline recommendation.[11-15] Barriers to guideline adherence have been identified, including the inability to access guidelines and physicians' attitude and belief toward the guidelines.[16] Pathman et al. reported that for the consistency between patient care and guidelines recommendations, physicians must be aware of, agree with, decide to adopt (i.e. decide it is appropriate and feasible to use in their own practice), and adhere to the recommendations (i.e. actually follow them for appropriate patients at the appropriate time).[17,18] Several studies have been conducted based on this 'awareness to adherence' model, yet only one came from developing countries.[17]

We would like to know whether this model applies also for a developing country like Indonesia. In this study we explore the degree of general practitioners' awareness of agreement with, adoption of and adherence to the type 2 diabetes mellitus guidelines in Indonesia, and identify associated physicians' characteristics.

Methods

Questionnaire design and data collection

Based on the evaluation of hypertension guidelines questionnaire by Heneghan et al.[19], we developed a similar questionnaire centered on items in the Consensus on the Management of Type 2 Diabetes Mellitus 2011 of the Indonesian Society of Endocrinology.[7] We included questions on the respondent characteristics: gender, age, specialization, practice duration, type of practice, location of practice, previous participation on type 2 diabetes management training and number and proportion of diabetes patients seen in their practice. According to the guideline recommendations we grouped

the questionnaire content into screening, diagnosis, treatment, life-style modification, management of co-morbidities and diabetes complications (Table 1). For the nominal and ordinal response options we followed the Pathman 'awareness-to-adherence' model, notably awareness (Yes/no), agreement (Yes/Unsure/No), and adoption (i.e. the recommendation is being followed in general in the appropriate patients; always/more than half/less than half/never). Adherence was assessed with an open ended question about the system responders had in place to promote or monitor the guideline application.

Table 1. Recommendations of the Indonesian type 2 Diabetes Mellitus guideline assessed in the questionnaire

	Statements in the guideline
Recommendation 1	Screening for type 2 diabetes should be performed in all patients with any of the risk factor listed in the guidelines.
Recommendation 2	In patients with classic DM symptoms, one random blood (plasma) glucose test with result >200 mg/dL is enough to confirm the diagnosis.
Recommendation 3	For newly diagnosed patients, management should be started with meal planning and exercise for 2–4 weeks.
Recommendation 4	Sulfonylurea is the drug of choice for normal and underweight patients.
Recommendation 5	Most patients should achieve Fasting Blood Glucose (FBG) of <100 mg/dL and 2-hour post-prandial Blood Glucose (2-h pp BG) of <140 mg/dL.
Recommendation 6	Blood pressure should be reduced to below 130/80 mmHg.
Recommendation 7	Statin should be prescribed to people with type 2 diabetes who are over 40 years old or have CVD risk.

The questionnaire was pilot tested to five GPs from the Community Medicine Department of the Faculty of Medicine Universitas Indonesia to determine whether the questions were clear, understandable, and in a logical order (face validity). Moreover the same GPs and three endocrinologists who are familiar with the diabetes guideline were asked to criticize the content of the questionnaire (content validity). Based on the results of this pilot, minor

changes were made. Further psychometric evaluation of the reliability was not performed.

The final questionnaire was distributed to all physicians attending the Indonesian Association of Family Practitioners annual conference on November 2012 in Jakarta, Indonesia. The questionnaire was put in the delegates pack together with an information leaflet on consent for survey participation. Returning of the self-completed questionnaire by responders was seen as their token of consent. Before handing out their certificate of attendance conference participants were informed about the possibility of participation. The Health Research Ethics Committee of the Faculty of Medicine Universitas Indonesia reviewed and approved the study.

Analyses and coding of data

We explored the association between respondent characteristics and adherence to each of the seven guideline recommendations. For this we used multivariate logistic regression analysis. To prevent for a type 2 error, only GP characteristics with a univariate p-value of 0.20 or less were selected for such multivariate analyses. The outcome for these data analyses was the number of responders' adherent to a recommendation. To prevent for spurious findings at least 10 participants adherent to the recommendation were needed for each respondent characteristic included in the multivariable analysis.[20] We used SPSS, version 20.0 for Windows (SPSS Inc., Chicago, IL, USA) for all data analysis.

Responders were classified as 'unaware of a recommendation' if they answered "no" on the question on familiarity with that recommendation. Agreement was classified according to whether they agreed or not with the guideline. They were considered to have adopted a guideline when they reported implementing it 'more than half of the time'. They were considered

to adhere to the recommendation when they 'always' or 'more than half of the time' applied it in clinical practice and specified the system they used to promote or monitor application. The proportions of doctors who were aware of, agreed with, adopted and adhered to each recommendation were calculated over the total number of responders.

Years of practice experience was grouped in 15 years or less and more than 15 years. The Perkeni guideline was firstly introduced in 1993. Therefore we assume that GPs who practiced less than 15 years should be aware of the guideline during their medical training.

We assumed the missing outcome data to represent no awareness, no agreement, no adoption and no adherence. For respondent characteristics with up to 15% missing data, we used conditional imputation, imputing the mean or median. We used mean and median values for imputation since we thought we had not the proper participant characteristic's to do regression analyses for imputation.

Results

From the 662 conference participants, 414 questionnaires (63%) were collected. We included 399 (96%) questionnaires from GPs and excluded 3 questionnaires from specialists and 12 from other health care professionals (e.g. nurses and dietician/nutritionists). The missing data for awareness, agreement, adoption and adherence ranged from none to 10%. Adherence to screening had no missing data, while the proportion of missing data for adherence to statin was highest (10%). Three participant characteristics had 5% or more missing data, with a maximum of 15% for number of diabetes patients seen in a week.

Characteristics of the GP responders are presented in Table 2. The higher proportion of them were female (68%), doing a solo (individual) practice (54%), practiced in Java-the most populated island in Indonesia (72%) and

had participated in diabetes management training (64%). Three-hundred forty of 383 GPs (89%) were aware of the consensus on the management of type 2 diabetes by the Indonesian Society of Endocrinology.

Table 2. Characteristics of the General Practice (GP) responders

Characteristics	n (%)	Mean (SD)	Min-max
Years of practice[a]		15.7 (8.8)	0-45 years
Gender[a]			
Male	126 (32)		
Female	273 (68)		
Practice type[a]			
Solo practice	215 (54)		
Private clinic	64 (16)		
Public health center	86 (22)		
Private hospital	20 (5)		
Public hospital (non academic)	8 (2)		
Academic hospital	6 (1)		
Practice location[c]			
Jakarta	119 (30)		
Outside Jakarta but within Java island	167 (42)		
Outside java	113 (28)		
Participation in DM training[b]			
Yes	234 (64)		
No	165 (36)		
Number of DM patients seen in a week[c]		13.0 (15.9)	1-120
Proportion of DM patients among all patients seen[a]			
<10%	261 (66)		
10-30%	117 (29)		
>30%	21 (5)		
Awareness to DM consensus[a]			
Never knew	43 (11)		
Heard but never had a copy	138 (36)		
Had but never read the consensus	78 (20)		
Has read and implemented it	124 (33)		

Missing data: a: <5%; b: 5-10%; c:>10-15%.

Figure 1 shows the proportions of the responders who were aware of, agreed with, adopted and adhered to the recommendations of the Indonesian type 2 diabetes mellitus guidelines. Awareness of each recommendation varied between 66 to 91% while agreement with varied between 41 to 87%. The least aware (265/399, 66%) and least agreed (163/399, 41%) recommendation was on the use of random blood (plasma) glucose test to diagnose patients with classic diabetes symptoms.

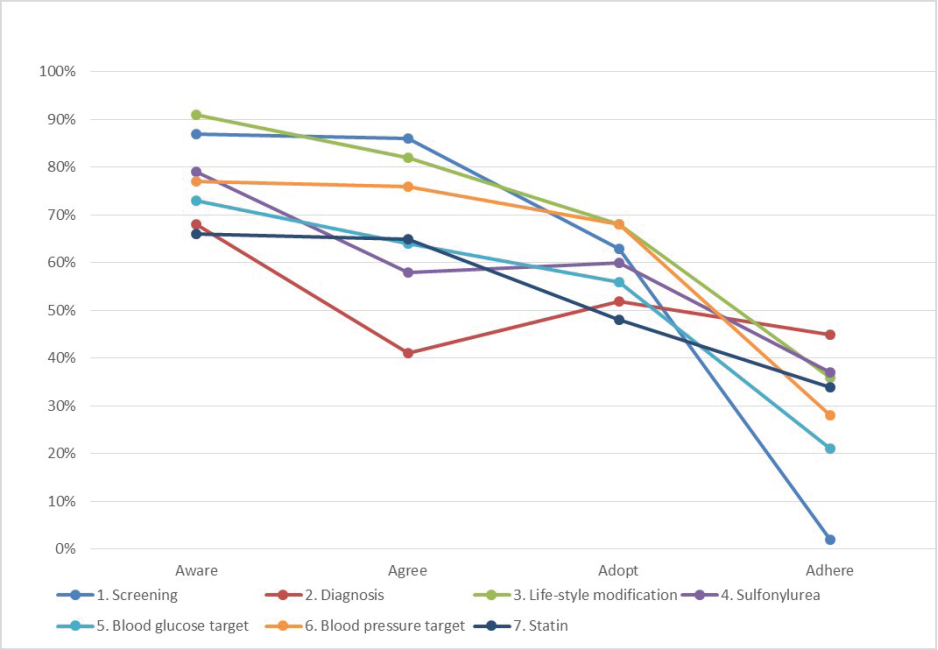

Figure 1. Proportions of awareness, agreement, adoption, and adherence of GPs (n = 399) to selected recommendations from the Indonesian type 2 Diabetes Mellitus (T2DM) guidelines.

Proportions (%) were computed based on the total GPs responders. Missing data was: <5% for screening (all), diagnosis (all), lifestyle modifications (awareness, agreement and adoption), and adherence on sulfonylurea. 5-10% for adherence on lifestyle modification, sulfonylurea (awareness, agreement and adoption), blood glucose target (all), blood pressure target (all) and statin prescription (all).

Adoption varied between 48 to 68%. The least adopted was statin use in type 2 diabetes who are over 40 years old or have CVD risk (192/399, 48%). Adherence varied between 2 to 45%, while the least adherence was on the recommendation to perform type 2 diabetes screening in patients with any risk factor listed in the guideline (7/399, 2%).

The summary of the univariate associations ($p \leq 0.2$) for six participant characteristics on adherence to the six recommendations can be found in Table 3 and the multivariate associations in Table 4. We were not able to investigate the presence of participant characteristics on the adherence to screening as the number of events was too small (7 events).

None of the participant characteristics were neither univariately nor multivariately associated with the recommendation on the diagnosis of diabetes (#2), Sulfonylurea for treatment (#4) and using blood pressure as treatment target (#6). During univariate regression analysis, years of practice, practice type and practice location, were associated with the recommendation on lifestyle modification (#3). However, none of these were retained during subsequent multivariate analysis. Only the proportion of diabetes patients was univariately associated with the recommendation on blood glucose as treatment target (#5).

During both univariate and subsequent multivariate analysis, adherence to the recommendation on statin prescription (#7) was found poor for responders with a practice prevalence of less than 10% diabetes patients (OR = 0.7, 95% CI 0.4;1.0, p = 0.08) and those practicing 15 years or less (OR =0.7, 95% CI: 0.4;1.0, p = 0.07) .

Table 3. Univariate associations (odds ratio and their 95% CI) between GPs (n = 399) characteristics and adherence to Indonesian type 2 Diabetes Mellitus (T2DM) guideline recommendations

	Diagnosis	Lifestyle modification	Sulfonylurea for treatment	Blood glucose target	Blood pressure target	Statin prescription
Adherent participants: n (%)	67 (45)	145 (36)	111 (37)	61 (21)	113 (28)	118 (34)
Characteristics						
Years of practice						
16 – 45*						
0 – 15	1.2 (0.8-1.7)[b]	1.4 (0.9-2.2)[c]	0.8 (0.6-1.3)[b]	0.8 (0.5-1.3)[c]	1.0 (0.7-1.6)[c]	0.7 (0.5-1.1)[c]
Gender						
Female*						
Male	1.1 (0.7-1.7)[a]	0.7 (0.5-1.2)[b]	1.3 (0.8-2.0)[a]	0.8 (0.5-1.4)[b]	0.8 (0.5-1.3)[b]	1.0 (0.6-1.6)[b]
Practice type						
Non solo practice*						
Solo practice	0.8 (0.6-1.2)[a]	0.7 (0.5-1.1)[c]	0.9 (0.6-1.3)[b]	1.0 (0.6-1.7)[c]	1.2 (0.8-1.9)[c]	1.0 (0.6-1.4)[b]
Practice location						
Outside Jakarta*						
Jakarta	0.9 (0.6-1.4)[c]	1.5 (1.0-2.3)[d]	1.0 (0.6-1.6)[c]	0.8 (0.5-1.4)[d]	1.1 (0.7-1.7)[d]	1.1 (0.7-1.7)[d]
DM training						
No*						
Yes	1.1 (0.7-1.7)[b]	1.3 (0.8-2.0)[d]	1.2 (0.8-1.9)[c]	1.0 (0.6-1.7)[d]	1.0 (0.6-1.6)[d]	1.1 (0.7-1.7)[d]
Proportion DM patients						
10% and above*						
<10%	1.0 (0.7-1.5)[b]	0.8 (0.5-1.2)[c]	0.9 (0.6-1.4)[b]	1.5 (0.9-2.5)[c]	1.1 (0.7-1.8)[c]	0.7 (0.5-1.1)[c]

Missing data: a:0- < 5%, b:5-10%, c:>10-15%, d:>15-19%. *reference.
Adherence to screening was not included in the univariate analysis since the number of events were too small (seven events).
Associations which have p value <0.2,
• Life-style modification: years of practice, practice type, practice location.
• Blood glucose target: proportion of diabetes patients.
• Statin: years of practice, proportion of diabetes patients.
• Diagnosis, sulfonylurea for treatment and blood pressure target: none.

Table 4. Independent associations (multivariate odds ratio and their 95% CI) between GPs (n = 399) characteristics and adherence to Indonesian type 2 Diabetes Guidelines recommendations

	Lifestyle modification		*Blood glucose target*		*Statin prescription*	
Characteristics	**OR (95% CI)**	**p**	**OR (95% CI)**	**p**	**OR (95% CI)**	**p**
Years of practice						
16 – 45*						
0 – 15	1.2 (0.7-2.2)[c]	0.50	-		0.7 (0.4-1.1)[c]	0.07
Gender						
Female*						
Male	0.9 (0.5-1.4)[b]	0.51	-		-	
Practice type						
Non solo practice*						
Solo practice	0.9 (0.5-1.3)[c]	0.51	-		-	
Practice location						
Outside Jakarta*						
Jakarta	1.3 (0.8-2.1)[d]	0.29	-		-	
DM training						
No*						
Yes	-		-		-	
Proportion DM patients						
10% and above*						
<10%	0.8 (0.5-1.3)[c]	0.37	1.5 (0.9-2.5)[c]	0.16	0.7 (0.4-1.1)[c]	0.08

Missing data: a:0- < 5%, b:5-10%, c:>10-15%, d:>15-19%.
*reference.
Adherence to screening was not included in the multivariate analysis as the number of events were too small.
Adherence to recommendations on diagnosis, treatment and blood pressure target have no characteristic factors univariately associated (p-value ≤ 0.20) with them (see Table 2)

Discussion

This study shows that awareness and agreement of the GPs of the seven recommendations of the Indonesian type 2 diabetes mellitus guideline was quite high (66 to 91%). The high awareness of GPs and their familiarity with the guideline is most likely due to the extensive promotion and marketing efforts on the introduction of the Indonesian Society of Endocrinology guidelines. Despite this high awareness, a large number of GPs neither adopted nor adhered to the guideline recommendations. A practice prevalence of less than 10% diabetes patients and practicing 15 years or less were independently related with poor adherence to statin prescription.

Awareness – agreement – adoption and adherence to the recommendations

There was high awareness among responders on the need for screening for type 2 diabetes risk factors among those without diabetes symptoms. Still, most of our responders waited until several cardiovascular risk factors emerged in the patient before they advised a screening test to the patient or they did not have a system to identify patients with risk factors. This was indicated by an extremely low (2%) adherence to the screening recommendation for identification of type 2 diabetes. This result is in contrast with findings among GPs in Switzerland about their adherence to the screening of diabetes which reach 83%.[21]

We found the least agreement (41%) with the recommendation to use random blood (plasma) glucose in the diagnosis of diabetes in patients with classic diabetes symptoms. The majority of our responders believed it is more appropriate to examine patients with classic diabetes symptoms with a fasting plasma glucose test and 2-hour post-prandial plasma glucose test. Due to the fasting needed for these blood sugar tests, patients may delay or avoid the examination.

On statin prescription, we found that the level of awareness and adoption were the lowest (72% and 52%). With 32% adherence among our responders to the recommendation to prescribe statins, it is slightly higher than in a Seoul tertiary hospital (29%)[14] but much lower than the 68% adherence among Australian GPs[11]. Factors related to the adherence to the recommendation to prescribe statins in our study were more years of practice experience and larger proportion of diabetes patients the practice.

Adoption to guideline recommendations has been shown to be facilitated by the acquisition of the necessary knowledge and skills. High health costs for patients and practice, patient's knowledge, expectations, compliance, motivation and support for recommendation, lack of materials, logistic support and time of health professionals, and high proportions of patients without insurance have been reported as barriers to guidelines adherence.[16,17] Adherence to actions recommended in guidelines may require practice organization. Besides, adherence is facilitated when tools are in place to put the recommendations into practice.[22] A systematic review[17] reported a median adherence of 36% (Inter Quartile Range 30 to 56%) to recommendations from various guidelines. Our data reveal that adherence to all the recommendations was quite low since less than 50% responders did not implement a system to promote and monitor recommendations in their practice.

Our findings on the low adherence of the recommendation on screening and diagnosis may explain why two thirds of the diabetes population in Indonesian remain un-diagnosed[2]. The generally low adherence to the recommendations of the Indonesian guideline may partly explain the finding by Soewondo et al.[6] that 68% of patients in Indonesia diagnosed with diabetes were in poor glycemic control.

Pattern of leakage

Based on a systematic review on the utilization of clinical guidelines[17] we expected to find a consistent pattern of 'leakage', i.e. lower number

of positive responders, over the four subsequent steps of the Pathman's awareness-to-adherence model. In our study, adoption and adherence rates are generally progressively lower, except for the recommendations on diagnosis of diabetes and sulfonylurea treatment.

Our findings on the non-progressiveness of the recommendation on diagnosis of diabetes and sulfonylurea treatment deserve further consideration. As was stated previously, a majority of our responders believed that fasting and 2-hour post-prandial blood (plasma) glucose test are more appropriate than random blood (plasma) glucose in the diagnosis of diabetes in patients with classic diabetes symptoms. However, random blood glucose is more practical to be implemented in the practice so it is more adopted.

The Indonesian guideline recommends sulfonylurea as the drug of choice to manage hyperglycemia in normal and underweight type 2 diabetes patients. In all, 58% of our responders agree with this recommendation. In contrast to the Indonesian guidelines, the consensus statement of the American Diabetes Association and the European Association for the Study of Diabetes recommends simultaneous initiation of metformin and lifestyle intervention at diagnosis[10]. Familiarity with this ADA/EASD recommendation may cause some uncertainty, but metformin and other classes of blood glucose–lowering medications are not generally available in primary health centers[23]. This may explain why agreement with sulfonylurea as recommended treatment is lower than its adoption.

Strengths and limitations of the study

Our study supports the usefulness of the awareness-to-adherence model and provides valuable information on the utilization of an important guideline in Indonesia. Still, some aspects of our study, notably the sampling method, response rate of the survey, missing data and the use of self-reporting questionnaire, need further consideration.

Obtaining representative samples from the large number of Indonesian GPs, exceeding 70,000, who are distributed over the archipelago possess challenges for our type of research.

Recruitment of responders among those attending a conference in Jakarta (capital city of Indonesia) was seen as more practical although it might not represent physicians who do not have opportunity to attend such meeting. However, our responders represent GPs from all parts of Indonesia. Our response rate is within the range of that of similar studies as reported by the systematic review of Mickan et al[17].

Self-reporting is the most simple and inexpensive method of measuring adherence. However, it has several limitations including over-estimation due to recall bias and social desirability bias.[24] These drawbacks have been addressed through determination of specific time period in the questionnaire, assessment of specific behavior related to the recommendations, non-judgmental statements and confidentiality.

The awareness-to adherence model may help to identify GPs' specific concerns with recommended practice changes. If uptake of a specific recommendation is low, qualitative approach to the concerns and barriers might be useful. Implementation of a quality assurance system which could further illustrate the care being received by diabetes patients in relation to the clinical outcomes is believed to be beneficial to promote adherence to guideline recommendations and increase the quality of diabetes care.[25]

Conclusions

Our study shows that high awareness of the guideline does not always lead to adoption nor adherence to its recommendations. The production and dissemination of guidelines alone is not sufficient to ensure that research

evidence gets into practice. Improvement of clinicians' awareness of, agreement with, and adoption to guidelines need to be incorporated in to strategies to improve guideline adherence.

Competing interests

IS coordinated several diabetes projects of the Indonesian Society of Endocrinology. PS is the past president of the Indonesian Society of Endocrinology. YvdG, PG and GvdH have no competing interest.

Authors' contributions

GvdH (guarantor) and YvdG had the original idea, and with ISW and PG, designed the study. ISW and PS were responsible for data collection. ISW wrote the original draft of the manuscript, and all authors contributed to the concept and also all revised drafts of the manuscript. All authors read and approved the final manuscript.

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Chapter 4

Adapting clinical guidelines in low-resources countries: a study on the guideline on the management and prevention of type 2 diabetes mellitus in Indonesia

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Abstract

Background - *Most of the clinical guidelines in low-resource countries are adaptations from pre-existing international guidelines. This adaptation can be problematic when those international guidelines are not based on current evidence or original evidence-based international guidelines are not followed. This study aims to evaluate the quality of an Indonesian type 2 diabetes guideline adapted from selected international guidelines.*

Methods - *The "Consensus on the Management and Prevention of type 2 Diabetes in Indonesia 2011" is a guideline by the Indonesian Society of Endocrinology (Perkeni). Four parent guidelines identified from its list of references were from the International Diabetes Federation (IDF), American Association of Clinical Endocrinologist (AACE), American Diabetes Association (ADA) and one jointly released by ADA and European Association for the Study of Diabetes (EASD). Two reviewers independently assessed its quality using the Appraisal of Guidelines, Research and Evaluation Collaboration (AGREE II) instrument. Six recommendations were compared: (1) screening for diabetes; (2) diagnosis; (3) control of hyperglycemia; (4) target blood glucose; (5) target blood pressure; (6) and treatment of dyslipidemia.*

Results - *Perkeni's guideline satisfied 55% of the AGREE II items, while its parent guidelines satisfied 59% to 74%. Perkeni's shows low score on "rigor of development" and "applicability" and the lowest score in the "scope and purpose" domain. Differences were found in four recommendations: the screening of diabetes, control of hyperglycemia, target blood glucose and treatment of dyslipidemia. In three out of those four, Perkeni followed the ADA's recommendation.*

Conclusion - *Derivation of recommendations from parent guidelines and their adaptation to the context of Indonesian health care lacks transparency. When guidelines are either derived from other guidelines or adapted for use in different context, Evidence-based Practice principles should be followed and adhered to.*

Introduction

A clinical practice guideline is defined as "systematically developed statements to assist practitioner and patient decisions on appropriate health care for specific clinical circumstances".[1] It is seen as a way to translate evidence from research to clinical practice and its production and utilization are remarkably increased over the past few decades. One of the many benefits of guidelines is to improve the consistency of care. However, guidelines developed by various institutions for similar health problems may result in conflicting recommendations.[2]

To ensure the quality of the guidelines, transparency on the development process is considered crucial, in particular a rigorous approach to the development is needed and various skills and experts should be involved.[3,4] For some institutions, especially those in developing countries, the availability of such resources is often limited.[5,6] A recent systematic review on diabetes guidelines in non-western countries found that 79% of the guidelines were based on recommendations from other national or international guidelines.[7] Nevertheless, an adaptation of a guideline produced in one cultural and organizational setting for use in another setting (trans-contextual adaptation[8]) needs to ensure that the resulting and final recommendations could still preserve its validity.

The overall aim of adaptation is to take advantage of existing guidelines in order to enhance the efficient production and use of high-quality adapted guidelines.

Several approaches to adoption and adaptation of guidelines to local situation have been proposed and endorsed, such as the ADAPTE collaboration[9] and the "Systematic Guidelines Review method"[10]. Basically, the approaches should involve systematic search and selection of guidelines, a quality assessment of the guidelines, and a transparent approach during recommendation

formulation, plus an external peer-review and a formal endorsement procedure. While this approach involves relatively complex processes and certain expertise, these are scarce sources in low-resources countries.

In Indonesia, the adoption and adaptation of international guidelines has also been chosen as a pragmatic and practical approach to guideline development. Currently the number of clinical practice guidelines in Indonesia is less than 20. Although no data is available, observation by the author revealed that all of the guidelines were developed using that approach. One such clinical guidelines is the so-called "Consensus on the Management and Prevention of type 2 Diabetes in Indonesia" of the Indonesian Society of Endocrinology (Perkeni guideline). The guideline was first released in 1993 and has been updated five times in the last 10 years.[11] Using the Indonesian type 2 diabetes guideline as a case study, this study aim to analyze a guideline of a national body from a low resource country to assess if the guideline has been developed appropriately and have recommended appropriate conclusions.

Methods

Retrieval of guidelines

For this case study, we used the fifth edition of the Indonesian type 2 diabetes guideline by the Indonesian Society of Endocrinology (published in 2011). Recommendations adapted from the parent guidelines were included in the Perkeni guideline based on a consensus from the members of the Indonesian Society of Endocrinology.

Four guidelines were listed as the parent guidelines: the Global Guideline for type 2 Diabetes by the International Diabetes Federation 2005[12], the Medical Guidelines for Clinical Practice for Developing a Diabetes Mellitus Comprehensive Care Plan 2007 by the American Association of Clinical Endocrinologist[13], the Medical Management of Hyperglycemia in Type 2

Diabetes: A Consensus Algorithm for the Initiation and Adjustment of Therapy of the American Diabetes Association and the European Association for the Study of Diabetes[14] and the Standards of Medical Care in Diabetes – 2010 by the American Diabetes Association[15]. We retrieved the original full version of the parent guidelines from the website of the issuing institute or society.

Quality appraisal of the guidelines

Two reviewers (IS and GW) who were not involved in the development of any of the guidelines independently assessed the quality of the guidelines using the modified version of the instrument developed by the Appraisal of Guidelines, Research and Evaluation Collaboration (AGREE II).[16] The AGREE II instrument contains 23 key items organized in six methodological domains: scope and purpose (items 1-3), stakeholder involvement (items 4-6), rigor of development (items 7-14), clarity of recommendations (items 15-18), applicability (items 19-21), and editorial independence (items 22-23). The AGREE instrument is sensitive for differences in important aspects of guidelines, can be used consistently and easily by a wide range of professionals from different backgrounds, and has acceptable reliability for most domains. The instrument uses a seven-point response scale (strongly agree [7] to strongly disagree [1]) for each item). The assessors then compared their individual scores for each item and came to consensus on discrepant scores (defined as scores varying by three points or more on the seven-point AGREE II scale). If the two assessors were unable to reach consensus, opinion from a third person (GvdH) was sought and opted as the final decision. If the two assessors' scores differed by two points they were averaged; if they differed by one point the lower score was kept. Standardized domain scores (expressed on a scale of 0–100) were calculated using the approach of AGREE II ([obtained score – minimum possible score] divided by [maximum possible score – minimum possible score]).[17] Interview with the person responsible for the development of the current

Perkeni guideline was conducted by the principal investigator (IS) to obtain more insight into the guideline development process.

Comparison of adopted guideline with its parental guidelines

We identified six major clinically relevant recommendations from the Perkeni guideline: (1) the screening of diabetes; (2) the diagnosis of type 2 diabetes; (3) the control of hyperglycemia; (4) the target blood glucose; (5) the target blood pressure; (6) the treatment of dyslipidemia. IS and GW extracted the major clinically relevant recommendation from the guidelines. IS and GW compared the similarity of each recommendation statement with the four parent guidelines. For each major recommendation in Perkeni we also assessed which parent guidelines was followed (i.e which recommendation has been adopted). In addition, we identified and checked citations of the original research used as the source for each recommendation in the parental guidelines. We identified the highest quality of study design among the references as the representative level of evidence for each recommendation.

Results

The guidelines

Three of the parent guidelines (IDF, AACE and ADA) made general recommendations on the medical treatment and early identification of complications and co-morbidities of diabetes. Meanwhile, the joint consensus of the ADA and EASD focused on the pharmacologic intervention for hyperglycemia (see table 1).

The recommendations of the ADA, AACE and ADA-EASD guidelines are based on a combination of expert opinion and literature reviews. IDF guideline is the only guideline that had no explicit reference to expert opinions/consensus or clinical judgment.

The IDF, ADA-EASD and Perkeni guidelines did not provide their method for assessment and rating of evidence. The Perkeni, IDF and ADA-EASD guidelines did not grade the recommendations. ADA classified their grade of recommendations into five groups with "A" being the highest grade which incorporates clear evidence from well conducted RCTs or meta-analysis with quality ratings and "E" being the lowest as it is based on expert consensus or clinical experience. On the other hand, AACE have four categories of recommendations where grade "A" recommendation is the one supported by homogenous evidence from >1 RCTs or meta-analysis with quality ratings and grade "D" when no conclusive studies are available to support the recommendation.

Quality of the guidelines

Table 2 shows the overall wide variation in the fulfillment of the AGREE II items for all of the guidelines. Still, all guidelines attained scores higher than 80% in the "clarity of presentation" domain. Yet, in all other domains the scores varied considerably and in the "rigor of development" domain only IDF guideline obtained a score higher than 50% while in the "applicability" domain all guidelines obtained scores lower than 40%. Compared to the other guidelines, Perkeni guideline has the lowest quality in all AGREE II domains except for "scope and purpose".

During the interview, it was found that the process of developing the guideline by Perkeni was usually started with one small team consisted of one or two experts supported by one or two technical team members developing the first draft. Rigorous and systematic searching on the identification of the source guidelines was lacking, as was appraisal of the quality of the original research that was used as the source for each recommendation in the parental guidelines. The draft of the guideline was then presented several time in society meetings to gain consensus. Meanwhile, the guideline development team searched for evidence to support the agreed recommendations.

Table 1. Characteristics of the parent guidelines of the Indonesian type 2 diabetes guideline

Title	Publisher	Country, language	Publication Date	Guidelines scope	Basis for the recommendation
Global guidelines for type 2 diabetes(1)	International Diabetes Federation (IDF)	International, English	2005	Diagnosis (of diabetes and complications), Therapy (of hyperglycemia, complications and co-morbid)	RCTs and other primary studies; systematic reviews or other reviews; guidelines
Medical guidelines for clinical practice for developing a diabetes mellitus comprehensive care plan(2)	American Association of Clinical Endocrinologist (AACE)	US, English	May 2007	Diagnosis (of diabetes and complications), Therapy (of hyperglycemia, complications and co-morbid)	RCTs and other primary studies; systematic reviews or other reviews; guidelines; expert opinion/ consensus
Medical Management of Hyperglycemia in Type 2 Diabetes(3)	American Diabetes Association (ADA), European Association for the Study of Diabetes (EASD)	US and European Union, English	Jan 2009	Therapy (of hyperglycemia; focus on pharmacotherapy)	RCTs and other primary studies; systematic reviews or other reviews; guidelines, clinical judgment
Standards of medical care in diabetes(4)	American Diabetes Association (ADA)	US, English	Jan 2010	Diagnosis (of diabetes and complications), Therapy (of hyperglycemia, complications and co-morbid)	RCTs and other primary studies; systematic reviews or other reviews; guidelines; clinical judgment

Table 2 Score achievement (%) of the type 2 diabetes guidelines based on Appraisal of Guidelines, Research and Evaluation Collaboration (AGREE) II items.

Domain	IDF	AACE	EASD-ADA	ADA	Perkeni
Scope and purpose	47	67	56	39	72
Stakeholder involvement	53	64	53	50	33
Rigour of development	57	42	28	46	0
Clarity of presentation	97	89	100	97	92
Applicability	38	0	10	13	17
Editorial independence	88	25	25	33	0

Data presented are AGREE II scores (0-100; low scores reflect poor quality). Each item was rated on a seven-point Likert scale that measured the extent to which an item was fulfilled: 1-strongly disagree to 7-strongly agree. Scores were standardized within domains by dividing the difference between the consensus score and the minimum possible score by the difference between the maximum and minimum possible scores.
IDF=International Diabetes Federation; AACE=American Association of Clinical Endocrinologis; EASD=European Association for the study of Diabetes; ADA=American Diabetes Association

Comparison of the recommendations with PERKENI guideline

Table 3 shows the source of the Indonesian guideline recommendations and the highest level of the study design used to build the recommendation in each parent guideline. Recommendations for the management of type 2 diabetes were rather similar across the parent guidelines, but the detail varied.

Perkeni and all parent guidelines have similar criteria to diagnose diabetes (based on the presence of classic diabetes symptoms and blood glucose or HbA1c measurement) and recommend that blood pressure should be lowered below of 130/80 mmHg.

Differences between the parent guidelines were found in four areas: screening for diabetes, control of hyperglycemia; blood glucose target and dyslipidemia management.

Screening for diabetes - All parent guidelines agreed that the screening of asymptomatic patients for diabetes should be targeted to high risk adults. Differences existed in defining those at risk especially in-terms of age group and nutrition status. In the AACE guideline, an individual aged above 30 should be screened for any diabetes' risk factors. According to the ADA guideline, age over 45 and nutritional status are preconditions for screening while the IDF provides no information. Perkeni adopted ADA screening recommendation for individuals who are overweight/obese or aged over 45.
Control of hyperglycemia – ADA, AACE and ADA-EASD guidelines recommend initiation of pharmacologic intervention (metformin) for the control of hyperglycemia simultaneously with life-style modification. Perkeni adopted a recommendation from IDF which recommends pharmacologic intervention for control of hyperglycemia when target blood glucose is not achieved. However, the IDF recommendation did not mention a time-period for this target.

Blood glucose target - Perkeni recommends a somewhat lenient blood glucose target of HbA1c<7 compared to HbA1c<6.5%. This is an adoption of the ADA and ADA-EASD recommendations.

Dyslipidemia management - All guidelines recommend statin as a preferable treatment, but for different specific indications. IDF and ADA guidelines recommend statin prescription based on age group (above 40 years) and the presence of CVD or CVD risk factors, regardless of baseline lipid levels. The AACE recommends taking baseline lipid levels and prescribing statins when needed to achieve certain target lipid levels. Perkeni recommendations were adopted from IDF and ADA guidelines.

Comparison of linked citations

Citations of similar recommendations - The recommendation on the diagnostic criteria in ADA guideline was derived from their own expert committee report from 1997. IDF cited the 2003 version of ADA expert

committee report and a WHO report in 1999, while AACE made their recommendation based on a 2006 joint report of WHO and IDF.

The recommendation on the blood pressure target was made based on guidelines from various institutions. The citation that was cited by three parent guidelines (AACE, ADA and IDF) was the 7th report of the Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7).[18] Both ADA and IDF also cited similar trials by Hanson et al (Hypertension Optimal Treatment study)[19] and UK Prospective Diabetes Study (UKPDS) 38.[20]

Citations of different recommendations -The recommendation from ADA and AACE on the importance of screening of high risk individuals for diabetes was made based on their own independent literature review. Only IDF cited primary studies such as the UKPDS[21] and a population study by Harris et al[22], in addition to WHO consultation report.[23] However, no further references could be traced from the three guidelines on the risk factors which warrant screening.

Three guidelines (AACE, ADA and ADA-EASD) were in agreement about the use of pharmacologic treatment simultaneously with life-style modification on newly diagnosed diabetes patients. In this case, ADA merely cited the latest and previous ADA-EASD recommendation while AACE based their recommendation on a trial by Esposito et al[24] and the Diabetes Control and Complications Trial (DCCT)which was conducted on type 1 diabetes.[25] ADA-EASD agree that metformin therapy should be initiated concurrently with lifestyle intervention at diagnosis based on the clinical judgement that for most individuals with type 2 diabetes, lifestyle interventions fail to achieve or maintain the metabolic goals either because of failure to lose weight, weight regain, progressive disease, or a combination of factors. AACE also included the report from Diabetes Prevention Program

Research Group[26] which described superior effectiveness of lifestyle to metformin. Despite all the clinical trials results, AACE recommendation was in the end made based on clinical judgment. IDF recommendation that pharmacologic intervention should be given when target blood glucose is not achieved by life-style modification was adopted from several other guidelines[27-30] and the UKPDS trial.[31]

ADA recommendation on blood glucose target of HbA1c<7 was made based on several trials including the ACCORD trialwhich demonstrated no benefit of intensive glycemiccontrol on CVD outcomes.[32] The source of recommendation on blood glucose target from the latest ADA-EASD was the 2008 version of the ADA guideline.[33] Among the two guidelines (AACE and IDF) which has recommended lower HbA1c target (<6.5), the only common source being used is the prospective observational UKPDS 35 study.[34] While AACE cited several other trials and observational studies in their 2006 Consensus Conference Report[35] for this recommendation, IDF cited systematic review of prospective observational studies by Laakso et al[36] and Selvin et al[37]; together with several guidelines including the 1999 IDF guideline.[38] Both AACE and IDF did not include the ACCORD trial as the study was published after both guidelines have been released.

Several trials were cited by three parent guidelines (AACE, ADA and IDF) to recommend that statins are the pharmacologic treatment of choice for lipid management of diabetes patients; the commonly cited reference were the Heart Protection Study (HPS)[39] and the Collaborative Atorvastatin Diabetes Study (CARDS).[40] Several other guidelines were also cited by the AACE and IDF on their recommendation on statins.

Table 3. Comparison of the recommendations in the Perkeni guidelines and the parent guidelines and the level of the evidence supporting the recommendations

	Recommendations from the parent guidelines; (*levels of evidence*)				**Perkeni recommendation**	**Parent guidelines from which recommendation is derived**
Topics	**AACE**	**ADA**	**IDF**	**ADA-EASD**		
Prevention	Annually screen all individuals 30 years or older with any of the listed risk factors (overweight/ obese among others)	Testing should be considered in all adults who are overweight (BMI 25 kg/m2) and have additional risk factors	Detection programs should target high-risk people identified by assessment of risk factors* *the risk factors is not clearly stated;	N.A	Testing should be considered in all adults with any of the listed risk factors (age>45 and BMI >23 among others).	AACE and ADA
Strength of the recommendation (as stated in each respective guidelines)	Grade B	grade B	not provided			
References	AACE Consensus Conference (2006); Experts' consensus based on literature review	Engelgau et al (2000); technical review with cost-benefit analysis	WHO report (2003), UKPDS 6 (1990), Harris (1992, cohort study)			
Levels of evidence (Oxford CEBM 2009)						

	Recommendations from the Parent guidelines; (*levels of evidence**)				Perkeni recommendation	Parent guidelines from which recommendation is derived
Topics	**AACE**	**ADA**	**IDF**	**ADA-EASD**		
Diagnosis	FBG > 126 or Random BG > 200 for those with classic DM symptoms. Positive BG only without symptoms, should be repeated	FBG > 126 or Random BG > 200 for those with classic DM symptoms. Positive BG only without symptoms, should be repeated	FBG > 126 or Random BG > 200 for those with classic DM symptoms. Positive BG only without symptoms, should be repeated	N.A	FBG > 126 or Random BG > 200 for those with classic DM symptoms. Positive BG only without symptoms, should be repeated	All similar
Strength of the recommendation (as stated in each respective guidelines)	Grade B	not provided	not provided			
Evidence	WHO/IDF (2006); Experts' consensus based on literature review	ADA Expert committee report (1997)	WHO report (1999), ADA expert committee report (2003)			
Levels of evidence (Oxford CEBM 2009)						

	Recommendations from the Parent guidelines; (*levels of evidence**)				Perkeni recommendation	Parent guidelines from which recommendation is derived
Topics	**AACE**	**ADA**	**IDF**	**ADA-EASD**		
Control of hyperglycemia	After diagnosis, life-style modification is advised simultaneously with pharmacologic treatment	After diagnosis, life-style modification is advised simultaneously with pharmacologic treatment (i.e. metformin)	Begin oral glucose-lowering drugs when lifestyle interventions alone are unable to maintain blood glucose control at target levels	After diagnosis, life-style modification is advised simultaneously with pharmacologic treatment	After diagnosis, start with life-style modification 2-4 weeks. Pharmacology may be given if target blood glucose is not achieved.	IDF
Strength of the recommendation (as stated in each respective guidelines)	grade A	not provided	not provided	consensus		
Evidence	Esposito K, et al (2004), DCCT (1993), Esposito K, et al (2002), Ohkubo Y (1995), DCCT (2002) DCCT trial is conducted among type 1 DM using insulin as intervention	Nathan DM, et al (2006 and 2009); ADA-EASD consensus statement	CMA guidelines (2003), NICE guidelines (2001), Germany guidelines (2004), ICSI guidelines (2004) UKPDS 34 (1998)	RCTs: UKPDS (1998), DCCT (1993), ACCORD (2008), ADVANCE (2008), Diabetes Prevention Program Research Group (2005, lifestyle is more effective than metformin), Clinical judgement		
Levels of evidence (Oxford CEBM 2009)	1b		1a	1b		

	Recommendations from the Parent guidelines; (*levels of evidence**)				Perkeni recommendation	Parent guidelines from which recommendation is derived
Topics	**AACE**	**ADA**	**IDF**	**ADA-EASD**		
Blood glucose target	HbA1c<6.5;	HbA1c <7 and further below for selected individual	HbA1c<6.5	HbA1c <7	HbA1c <7	ADA and ADA-EASD
Strength of the recommendation (as stated in each respective guidelines)	grade B	grade A (microvascular complication prevention); B (macrovascular)	not provided	not provided		
Evidence	ACE/AACE consensus conference (2006).	Several trials such as the DCCT (1993), EDIC (follow up of DCCT, 2000), UKPDS (1998, and its follow up study 2008), Kumamoto (1995), ADVANCE (2008) and VADT (2009) ACCORD trial which shows the harm of further lowering of A1c (2008)	UKPDS 35 (2000), Laakso (1996), Selvin (2004), ADA guidelines (2004 and 2005), European diabetes policy group guidelines (1999), NICE guidelines (2001), CMA guidelines (2003)	ADA guidelines (2008)		
Levels of evidence (Oxford CEBM 2009)		1a	1a			

	Recommendations from the Parent guidelines; (*levels of evidence**)				Perkeni recommendation	Parent guidelines from which recommendation is derived
Topics	**AACE**	**ADA**	**IDF**	**ADA-EASD**		
Blood pressure target	<130/80 mmHg	<130/80 mmHg	<130/80 mmHg	N.A	130/80 mmHg	All similar
Strength of the recommendation (as stated in each respective guidelines)	grade A	grade C for systolic level and B for diastolic level	not provided			
Evidence	JNC7 Guidelines (2003),	JNC7 Guidelines (2003),	Diabetes Australia guidelines (2004), Canadian Diabetes Association guidelines (2003), ADA guidelines (2005), JNC guidelines (2003), European Hypertension Society guidelines (2003)			
	National Kidney Foundation consensus (2000).	Hanson et al (1998); Hypertension Optimal Treatment Trial UKPDS 38 trial (1998)	Hanson et al (1998); Hypertension Optimal Treatment Trial UKPDS 38 trial (1998)			
Levels of evidence (Oxford CEBM 2009)		1b	1a			

	Recommendations from the Parent guidelines; (*levels of evidence**)				Perkeni recommendation	Parent guidelines from which recommendation is derived
Topics	**AACE**	**ADA**	**IDF**	**ADA-EASD**		
Statin prescription	Statins are the pharmacologic treatment of choice No further detail whether it should be given according to or regardless of baseline lipid level	Statin therapy should be added to lifestyle therapy, regardless of lipid levels for diabetic patients ● with overt CVD. ● without CVD who are over the age of 40 years and have one or more other CVD risk factors.	a) statin for all >40 yr old (or all with declared CVD) b) statin for all >20 yr old with micro-albuminuria or assessed as being at particularly high risk	N.A	For patient who are >40 years old or have CVD risk, statin therapy should be added to lifestyle therapy, regardless of baseline lipid levels.	ADA and IDF
Strength of the recommendation (as stated in each respective guidelines)	grade A for statin recommendation	grade A	not provided			
Evidence	Grundy SM et al (National Heart Lung, and Blood Institute; American College of Cardiology Foundation; American Heart Association Guidelines 2004). Goldberg RB et al (CARE Trial, 1998) 10 trials (including HPS and CARDS) and 1 SR about statin	9 trials of statin: 4S (1997), HPS (2003), TNT (2006), ASCOT-LLA (2005), ASPEN (2006), CARDS (2004) and sub-analysis to those with high CVD risks (HPS and CARDS)	HPS trials (2003), CARDS trial (2004). Diabetes Australia guidelines (2004), Canadian Diabetes Association guidelines (2003), NICE guidelines (2002), SIGN guidelines (2001)			
Levels of evidence (Oxford CEBM 2009)	1a	1b	1a			

* levels of evidence listed in the guidelines was re-classified based on the Oxford 2011 Levels of Evidence for comparison within the matrix
N.A. = not applicable
Unclear = no rating of evidence is provided and no reference is linked to the recommendation.

Discussion

We found that the quality of the Indonesian diabetes guidelines is poor based on its low AGREE II score, especially in four area: stakeholder involvement, rigour of development, applicability and editorial independence. The reporting on the approach to its development lacked transparency. This in particular pertained to the derivation of the principal recommendations from existing guidelines and their adaptation to the context of the Indonesian health care. The interview with the Perkeni guideline developers confirmed important shortcomings in the approach. Hence, we report the rigor of the development as poor.

Discrepancies were found in four clinical recommendations: the screening of diabetes, the control of hyperglycemia, the target blood glucose and treatment of dyslipidemia. The majority of Perkeni guideline recommendations were derived from the ADA, which was the latest guideline published among the four parent guidelines although the AGREE II score was not the highest. Hence, adherence to Evidence-based Practice principles during its development can be questioned.

Our finding on the low AGREE II scores in each parent guideline, especially in the "Rigor of development" domain, means that generally those parent guidelines failed to show that they have conducted a systematic review on the best available evidences.[41] A previous systematic review which assessed the quality of 24 CPGs on diabetes management reported similar findings.[42] The review that examine the quality of CPGs that included recommendations on pharmacotherapy for glycemic control in type 2 diabetes indicated several guidelines that achieve higher score on the "rigor of development area" such as those developed by the UK National Institute for Health and Clinical Excellence, the Scottish Intercollegiate Guidelines Network and the American College of Physicians. Careful appraisal and selection of the

source guidelines is clearly paramount before adapting recommendations from one guideline to another.[43]

Several studies revealed that there are considerable variations and even conflicting recommendations concerning type 2 diabetes management from different guidelines.[44,45] Variation was believed to be due to insufficient evidence, differing interpretations of evidence, unsystematic guideline development methods, the influence of professional bodies, cultural factors such as differing expectations of apparent risks and benefits, socioeconomic factors, or the characteristics of the health care systems.[46] Our study revealed that even though all the source guidelines cited the same studies, yet they can come up with different recommendations. There is a higher chance that the (clinical) judgment of the guideline developer plays a dominant role in the final recommendations.

As expected, each of the guidelines used different sources. In the era where evidence-based clinical practice guidelines is reinforced, systematic searching of the evidence is considered a vital process in the guideline development. While sources included for recommendations in Perkeni have been taken from parent guidelines, transparency on and justification of their appropriateness is lacking. This was also a finding of Aarts et al. in their study on Obstructive Sleep Apnea-Hypopnea Syndrome guidelines.[47]

Although a wide range of diabetes guidelines existed, the most cited are guidelines from ADA, IDF, EASD and AACE.[7] This might explain the use of these four guidelines by Perkeni. In both ADAPTE collaboration[9] and the "Systematic Guidelines Review method",[10] the systematic search and selection of the guidelines, the quality assessment of the guidelines, and the transparent approach on the formulation of the recommendation are considered crucial steps in the guidelines adaptation process. However, we found no statement in the guideline that shows that this approach has

been followed by Perkeni. This was confirmed during the interview with the Perkeni guideline developers.

Engaging potential end users in the process of evaluating and adapting existing guidelines may help improve the uptake and utilization of the guideline.[48] This process has also been overlooked in the Indonesian type 2 diabetes guideline development, hence we found in our previous study that the adherence to the recommendations on the Indonesian type 2 diabetes guidelines is very low.[49]

As far as we know, this is a first study that examines how the recommendations from different guidelines were being adapted to develop a local diabetes guideline. Previous studies compared the quality and recommendations from different diabetes guidelines from different countries or different institutions.[42,44,45,50-52] While our findings only concern the Perkeni diabetes guideline they may hold true for other guidelines developed under similar conditions.

In this study, we minimized the observer bias during the assessment of the guideline quality through independent extraction and quality assessment by two researchers. While findings reported are mainly based on the literal or statements from the guidelines we only interviewed the developers of the Perkeni guideline.

Implementing evidence-based practice principles in guideline adaptation will help the efforts in low resource countries to improve their quality care practice through the use of high quality practice guidelines. In addition, these countries should aim to improve their capacity in assessing and selecting the guidelines as part of the adaptation process. In the future, the guideline could gain strength and quality by improving transparency in the process of guideline adaptation and by selecting guidelines that fulfil the AGREE II criteria at a high level to be adapted.

Conclusion

In view of the potential impact of CPGs on health care delivery and patient outcomes, it is crucial that clinical guidelines should be of optimal quality. The process underlying the Indonesian type 2 diabetes guideline development is curtailed due to being under-resourced and the use of the cited suboptimal source guidelines might risk the validity of the recommendations it contains. Implementation of evidence-based practice principles such as those proposed by ADAPTE collaboration should be adhered to when guideline are derived from other guidelines to be used in other than its original context or circumstances.

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Chapter 5

Quality and reporting of publications by Indonesian researchers: a literature survey

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Abstract

Aim *– To evaluate the quality of reporting of the risk of bias of the Indonesian medical research.*

Methods *– Publications from PubMed and non-PubMed indexed Indonesian medical journals between January 2008 to December 2010 were assessed for risk of bias based on criterion combination from Hedges-criteria and the Oxford Center for Evidence-based Medicine. We assessed whether the publications addressed the risk of bias adequately (quality of reporting) and whether the risk of bias criterion was fulfilled (quality of methods). The quality (both of reporting and of methods) of a study was classified as "high" if, for at least two-third of the criteria were adequately reported and fulfilled. It was classified as "low" when only one-third of the criteria were reported and or fulfilled.*

Results *– Of the 1753 publications, 29% (n=507) were original medical research. For 21% (109/507) the quality of reporting was high; for 15% (77/507) the quality of methods was high. The proportion of high quality was significantly higher among PubMed than non-PubMed indexed studies, with difference between proportions: 12% (95% CI of difference 3;23).*

Conclusion *– A small proportion of Indonesian studies have high quality reporting or methods. When international reporting guidelines are endorsed and followed, the quality of future studies may improve.*

Introduction

There is an increasing demand from the health professionals worldwide for Evidence-based Practice (EBP), i.e integrating clinical expertise with the best available research evidence along with patient preferences.[1, 2] Improving the evidence-base for diagnosis, etiology, prognosis and therapy holds great potential to increase the quality and efficiency of medical care. Increasingly discoveries of new approaches in care delivery and the comparative assessment of their impact on outcomes of disease and care, expand the possibilities for improving the health care and its cost-effectiveness. However, the abundant evidence is often not feasible for a clinician to handle. Insufficient information on the effectiveness of different options in patient management, can lead to the unnecessary, unproven, or even harmful delivery of services.

The future for EBP in the Asia pacific region is considered very promising even though it has only recently gained a relatively large scale interest in the region.[3] Implementation of EBP in that region has these notorious challenges: limited scientific resources, limited access to bibliographic databases and libraries, lack of time for trainings and attending workshops and lack of role models.[4] In addition, the research evidence from developing countries was frequently considered to be of lesser quality.[5, 6] Thus, evaluation on how the region performs so far in EBP is important. There are reports on quality of research in China[7] and India[8-10], yet, studies that evaluate the quality of research from Indonesia as one of the most populated country in the region is lacking.

In Indonesia, the concept of EBP has been actively disseminated in the past fifteen years.[3] This study aims to evaluate the quality of reporting of the risk of bias of the Indonesian medical research.

Methods

Selection of journals and articles

We searched PubMed for publications on medical research from Indonesia in the last three years (2008-2010), using the following search terms: Indonesia* [ad] AND (2010 [pdat] OR 2009 [pdat] OR 2008 [pdat]). In addition, we selected eight Indonesian general medical journals from the list of 21 high ranked (level B) accredited Indonesian journals of the Indonesian Ministry of Education in 2010.[11] These journals represented the health care journals that were read by Indonesian readers.

Together with a research assistant, the first author (ISW) retrieved electronic files and or the hard-copies of all the articles. We only included reports on original patient-oriented research or systematic reviews for further assessment. Patient-oriented research concerns studies on diagnosis, etiology, prognosis and therapy, including patients as research subjects, evaluating patient-oriented outcomes. General articles, such as editorials and letters, as well case reports and qualitative studies were excluded from the analysis. Although these types of publications may provide information important for EBP, they are generally not included in quantitative clinical epidemiology.[12] Studies that were not conducted by Indonesian researchers or had included only non-Indonesian subjects were also excluded. We classified publications according to the Hedges Project criteria for type of study: therapy, diagnosis, prognosis, etiology, economic evaluation, or systematic review (See appendix 1).[13, 14] Articles that did not fit into any of the Hedges project criteria were labeled as "other" and were excluded from further assessment. The selection and assessment of publications is presented in figure 1.

Study assessment

Each articles was randomly assigned to two of five reviewers (ISW, SRS, BWL, LA, and GW) who were trained in clinical epidemiology. They

assessed whether included publications addressed the risk of bias adequately (quality of reporting) and whether the risk of bias criteria were fulfilled (quality of methods). None of the reviewers (co)-authored the reviewed articles. The journal titles and names of the authors of the article were masked from the reviewers. They used slightly different assessment criteria for each study type (Appendix 2), which were based on a combination of the Hedges criteria[13] and the Oxford Center for Evidence-based Medicine critical appraisal worksheets.[15]

Each reviewer independently determined whether adequate information was given for each modified Hedges criterion (yes/no) and if, yes, whether it was fulfilled (yes/no). Disagreements were resolved by discussion and were based on full consensus among ISW, SRS, BWL and LA.

Data analysis

The quality of reporting of a study is determined by the number of adequately addressed risk of bias reporting criteria, and is judged as "high" if, for at least five (out of six or seven) adequate information was reported. The reporting quality of a study is judged as "low" when for less than three (out of six or seven) criteria adequate information was reported; in between it is judged as "moderate".

The quality of methods of a study is determined by the number of risk of bias criteria fulfilled. When a criterion is either not adequately reported or not fulfilled it may contribute to the risk of bias and reduces the quality of methods. The quality of methods of a study is judged as "high" when at least five of the six or seven methods criteria are fulfilled. The quality of methods of a study is judged as "low" when less than three criteria were fulfilled; in between it is judged as "moderate".

According to the type of study, we report for each criterion the number of studies that fulfill it and the number of studies that do not adequately report it (Table 2). The number of studies with high, moderate and low quality of reporting and quality of methods is reported in Table 3. In addition, we report the differences (with 95% confidence interval) in proportions between PubMed and non-PubMed indexed studies. The confidence interval calculations were based on the Newcombe-Wilson hybrid score methods. (16) A 95% confidence interval excluding zero denotes a statistically significant difference ($p<0.05$).

Results

Altogether, we screened 1759 articles: 581 articles were found from our search in PubMed and 1178 articles were retrieved from the eight journals that were listed in the list of Indonesian Ministry of Education. Among the PubMed indexed articles, we found 158 (28%) were published in the journal of the Indonesian Society of Internal Medicine (Acta Medica Indonesiana). The journal is the only journal from Indonesia that is currently indexed in PubMed. Four of the eight other Indonesian journals publish their articles in English; two journals in Indonesian language; and the rest publish in both English and Indonesian language. In the end, we included 507 articles of which 89 (18%) were indexed in PubMed. (Figure 1).

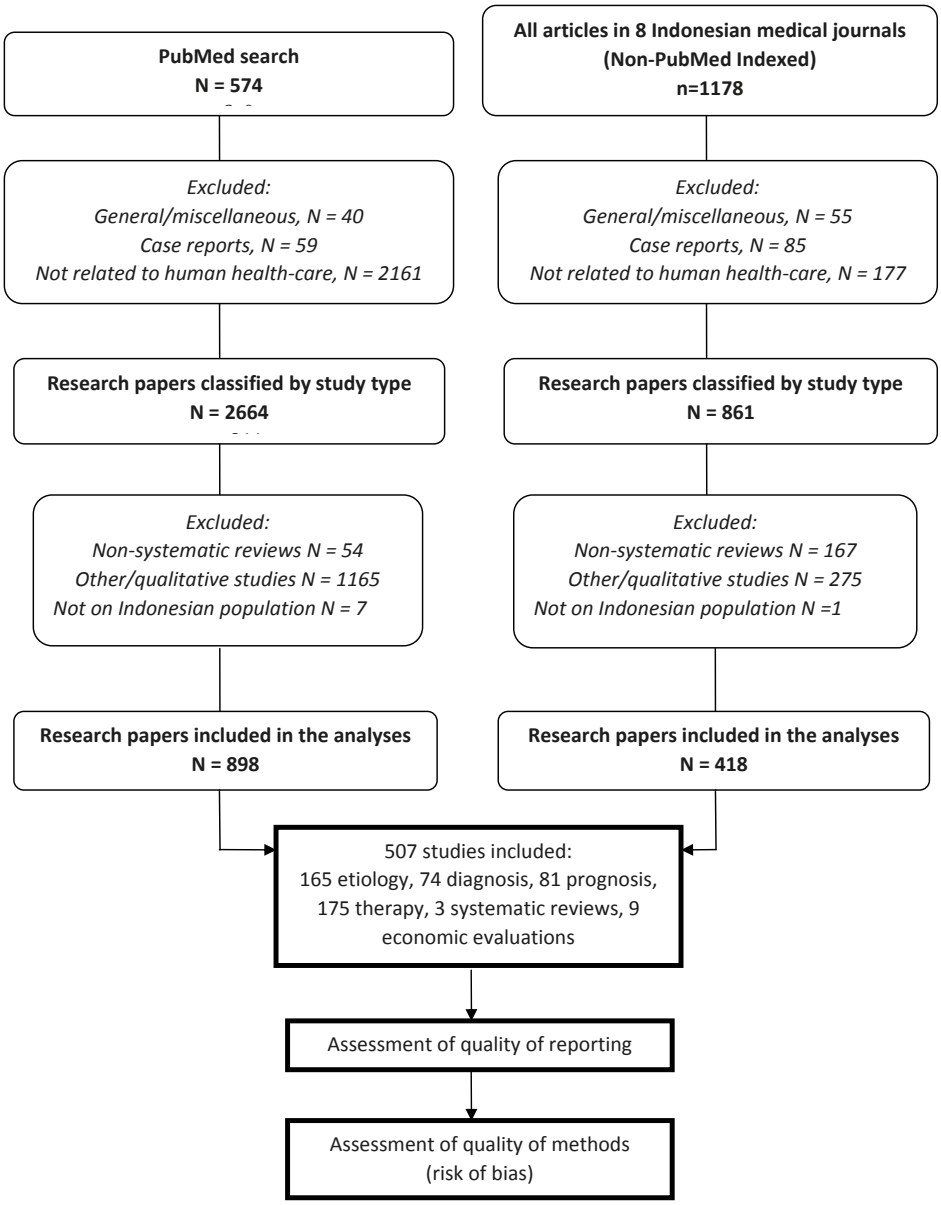

Figure 1. Flow diagram of the review process

Based on the Hedges Project criteria the most common study types were "therapy" (175/507, 35%) and "etiology" (165/507, or 33%). Distribution of the study types per journal is presented in Table 1.

Quality of reporting: addressing the risk of bias

From table 2, we can see that in each study type there were certain criteria which were not reported more frequently. In "etiologic" and "prognostic" studies more than 50% of the studies did not report about blinding of observers for outcome or exposure status. In "diagnostic" studies reporting of blinding of observers for reference standard or index test status also not reported by more than 50% of the studies. On the other hand "therapeutic" studies especially from non-Pubmed indexed journals were more often omitted the report on blinding of observers for treatment status (-34% difference; 95% CI -50;-18) and sufficient description of intervention (-15% difference; 95% CI -21;-9).

From table 3, we can see that of the 507 included articles, quality of reporting was low for 13 (3%) articles; moderate for 205 (50%) articles and high for 288 (57%) articles. None of the PubMed indexed publications were of low reporting quality.

Quality of methods: the risk of bias

Criteria on standardized measurement of both outcome and exposure status (etiology, prognosis and treatment), or index test and reference standard status (diagnosis) were fulfilled by more than 60% of the studies (table 2). Completeness of data were found on more than 50% of all type of the studies.

Further, 18% of the article (n=91) had a low quality of methods (high risk for bias); 67% (n=338) had moderate and 15% (n=77) had high quality (table 3). In general, PubMed indexed publications had a higher quality (22/89, or 25%) compared to those that were not indexed in PubMed (55/418, or 13%) and the difference was significant. Similar findings were also found among publications in different study types, but the differences were not significant. No low quality publications were indexed in PubMed, although significant difference was found only among "etiology" studies.

Table 1. Number (%) of articles in each journal published in year 2008-2010 that met the definition according to the Hedges Project criteria

Journals names	Number of articles	Articles included[a] (%)[b]	Etiology (%)[c]	Diagnosis (%)[c]	Prognosis (%)[c]	Therapy (%)[c]	Systematic Review (%)[c]	Economic evaluation (%)[c]
PubMed indexed								
Acta Medica Indonesiana	158	30 (19)	8 (27)	6 (20)	7 (23)	8 (27)	0	1 (3)
Non Indonesian journals[d]	417	59 (14)	7 (12)	6 (10)	14 (24)	24 (41)	2 (3)	6 (10)
Not PubMed indexed								
Folia Medica Indonesiana	153	36 (23)	9 (25)	6 (17)	6 (17)	15 (42)	0	0
Journal of the Indonesian Medical Association	248	59 (24)	24 (41)	9 (15)	6 (10)	20 (34)	0	0
Medical Journal of Indonesia	138	44 (32)	14 (32)	3 (7)	8 (18)	17 (39)	1(2)	1(2)
Media Medika Indonesiana	67	21 (31)	7 (33)	2 (9)	1 (5)	10 (48)	0	1 (5)
Paediatrica Indonesiana	204	124 (61)	41 (33)	27 (22)	16 (13)	40 (32)	0	0
Sari Pediatri	205	73 (36)	27 (37)	8 (11)	16 (22)	22 (30)	0	0
Universa Medicina	69	20 (29)	9 (45)	0	3 (15)	8 (40)	0	0
Majalah Kedokteran Bandung	94	41 (44)	19 (46)	7 (17)	4 (10)	11 (27)	0	0
Total	**1752**	**507 (29)**	**165 (33)**	**74 (15)**	**81 (16)**	**175 (34)**	**3(0)**	**9 (2)**

a Total articles included in assessment;
b total articles included in assessment (a) divided by number articles published in each journal.
c Number of articles divided by total articles included in assessment (a);
d Identified through PubMed

Table 2. Comparison of PubMed and non-PubMed indexed papers by reporting and fulfilment of each criterion for risk of bias.

Methods criteria	Not reported			Fulfilled[b]		
	PubMed	Non-PubMed	Difference[a]	PubMed	Non-PubMed	Difference[a]
Etiology	**n=15**	**n=150**		**n=15**	**n=150**	
Inception cohort	2 (13)	3 (2)	11 (-6;29)	3 (20)	32 (21)	-1 (-23;20)
Clearly identified comparison group(s)	2 (13)	6 (4)	9 (-8;27)	9 (60)	97 (65)	-5 (-31;21)
Completeness of data	2 (13)	8 (5)	8 (-10;26)	13 (87)	140 (93)	-7 (-24;11)
Blinding for outcome	13 (87)	98 (65)	21 (3;40)	2 (13)	20 (21)	-8 (-26;10)
Blinding for exposure	15 (50)	104 (69)	-19 (-46;7)	4 (13)	21 (14)	-1 (-19;17)
Standardized measurement of outcome	15 (50)	19 (13)	37 (11;63)	13 (43)	126 (84)	3 (-22;14)
Standardized measurement of exposure	0 (0)	23 (15)	-15 (-21;-10)	15 (100)	123 (82)	18 (12;24)
Diagnosis	**n=12**	**n=62**		**n=12**	**n=62**	
Comparison with reference standard	0 (0)	4 (6)	-6 (-13; 0)	11 (92)	53 (85)	6 (-12;24)
Completeness of data	1 (8)	2 (3)	5 (-11;21)	8 (67)	59 (95)	-28 (-56;-1)
Blinding for reference standard status	9 (75)	37 (60)	15 (-12;43)	1 (8)	13 (21)	-13 (-31;6)
Blinding for index test	7 (58)	41 (66)	-8 (-38;22)	5 (42)	12 (15)	27 (-2;56)
Standardized measurement of reference standard	1 (8)	7 (11)	-3 (-20;15)	11 (92)	55 (89)	3 (-15;20)
Standardized measurement of index test	0 (0)	7 (11)	-11 (19;-3)	12 (100)	53 (85)	15 (6;23)
Prognosis	**n=21**	**n=60**		**n=21**	**n=60**	
Inception cohort	0 (0)	4 (7)	-7 (-13; 0)	17 (81)	36 (60)	21 (0;42)
Completeness of data	6 (29)	16 (27)	2 (-20;24)	11 (52)	42 (70)	-18 (-42;7)
Blinding for outcome	12 (57)	41 (68)	-11 (-35;13)	9 (43)	16 (27)	16 (-8;40)
Blinding for exposure	16 (76)	48 (80)	-4 (-25;17)	4 (19)	4 (13)	6 (-13;25)
Standardized measurement of outcome	1 (5)	7 (12)	-7 (-19;5)	20 (95)	52 (87)	9 (-4;21)
Standardized measurement of exposure	2 (10)	12 (20)	-10 (-27;6)	19 (90)	48 (80)	10 (-6;27)
Treatment	**n=32**	**n=143**		**n=32**	**n=143**	
Random allocation	6 (19)	11 (8)	12 (-3;26)	14 (44)	83 (58)	-16 (-35;3)
Concealed treatment allocation	11 (34)	53 (37)	-2 (-20;17)	6 (19)	20 (14)	5 (-10;20)
Completeness of data	8 (25)	27 (19)	7 (-10;24)	17 (53)	106 (74)	-19 (-38; 0)
Blinding for treatment status	6 (19)	76 (53)	-34 (-50;-18)	13 (41)	21 (32)	7 (-12;25)
Standardized measurement of outcome	3 (9)	20 (14)	-4 (-16;8)	27 (84)	123 (86)	-2 (-16;12)
Sufficient description of intervention	0 (0)	22 (15)	-15 (-21;-9)	31 (97)	114 (80)	17 (8;26)

95% CI = 95 percent confidence interval for difference in proportion between PubMed and non-PubMed indexed papers per level of quality of reporting and methods

[a] A negative difference denotes a difference which is in favor of Non-PubMed indexed papers

[b] A criterion could only be fulfilled when information was reported and this information satisfied.

Table 3. Comparison of PubMed and non-PubMed indexed papers by quality of reporting and quality of methods according to study type

	Reporting quality			Methods quality		
	PubMed n (%)	**Non-PubMed** n (%)	**Difference**[a] % (95%CI)	**PubMed** n (%)	**Non-PubMed** n (%)	**Difference**[a] % (95%CI)
All	***n=89***	***n=418***		***n=89***	***n=418***	
High	45 (51)	243 (58)	-7 (-18;4)	22 (25)	55 (13)	12 (2;21)
Moderate	43 (49)	162 (39)	10 (-1;21)	54 (61)	284 (68)	-6 (-18;4)
Low	0	13 (3)	-3 (-5;1)	12 (14)	79 (19)	-5 (-13;3)
Etiology	***n=15***	***n=150***		***n=15***	***n=150***	
High	13 (87)	123 (82)	5 (-20;16)	1 (7)	7 (5)	2 (-11;15)
Moderate	2 (13)	23 (15)	-2 (-14;23)	14 (93)	127 (85)	9 (-5;23)
Low	0	4 (3)	-3 (-7;18)	0	16 (11)	-11 (-16;-6)
Diagnosis	***n=12***	***n=62***		***n=12***	***n=62***	
High	5 (42)	24 (39)	3 (-23;32)	5 (42)	15 (24)	17 (-12;47)
Moderate	7 (58)	37 (60)	-1 (-30;24)	6 (50)	40 (65)	-15 (-45;16)
Low	0	1 (1)	-2 (-9;23)	1 (8)	7 (11)	-3 (-20;15)
Prognosis	***n=21***	***n=60***		***n=21***	***n=60***	
High	8 (38)	16 (27)	11 (-10;35)	7 (33)	11 (18)	15 (-7;37)
Moderate	13 (62)	42 (70)	-8 (-31;13)	13 (62)	38 (63)	-1 (-26;23)
Low	0	2 (3)	-3 (-11;12)	1 (5)	11 (18)	-14 (-27; 0)
Treatment	***n=32***	***n=143***		***n=32***	***n=143***	
High	20 (62)	80 (56)	5 (-14;22)	7 (22)	22 (15)	4 (-11;19)
Moderate	12 (38)	60 (42)	-3 (-20;16)	17 (53)	79 (55)	0 (-20;19)
Low	0	3 (2)	-2 (-6;9)	8 (25)	42 (29)	-4 (-21;14)

A low level quality indicates that up to one-third of the criteria for quality were fulfilled/ reported.
A moderate level quality indicates that between one-third and two-third of the criteria for quality were fulfilled/reported.
A high level quality indicates that two-third or more of the criteria for quality were fulfilled/ reported.
95% CI = 95 percent confidence interval for difference in proportion between PubMed and non-PubMed indexed papers per level of quality of reporting and methods
[a] A negative difference denotes a difference which is in favor of Non-PubMed indexed papers

Discussion

In this study, we evaluated the quality of reporting and the quality of methods of patient oriented medical research published from January 2008 to December 2010 by Indonesian researchers. Overall, 21% of the 507 studies could be classified as having high quality of reporting and 15% having high quality of methods.

Patient oriented medical research may potentially support clinical practice's decision making. But such research concerned only 29% of the total volume of the retrieved Indonesian medical and health publications. When compared to India, about 36% of their health research publication related to clinical research.[10]

To our knowledge, we report the first evaluation of the quality of medical research articles from Indonesia. Thereby, we have added more data to the currently limited information on the quality of studies from low- and middle-income countries. Our study has some limitations. Among these was that we only searched for publications in PubMed and level B Indonesian journals, and restricted our analysis to the relatively small proportion of clinically-applicable research. Including other publication sources as well as fundamental and preclinical research would very likely have resulted in different findings. Even though we present the difference in proportion, we were aware that for some type of studies, the number of those published in PubMed was too small to allow statistical test. Still, we believe that our study provides a clear illustration about the quality of the published medical research by Indonesian researchers.

Currently, there are several high quality standards used globally including CONSORT statement for reporting interventional studies and STROBE statement for reporting observational studies. Another limitation of our study was that we arbitrarily chose to combine the Hedges Project criteria[13] and the Oxford Center for Evidence-based Medicine[15] for quality appraisal. The reason is that it has less criteria, hence more appropriate to evaluate the Indonesian research articles.

The proportion of Indonesian research published in indexed journals is unknown. Data from the Faculty of Medicine, Universitas of Indonesia, however show that annually about 600 studies are conducted by staff, residents

and students. Of these only 231 (39%) are published; 68 (11%) in international and 163 (27%) in local journals.[17] Moreover, Indonesian researchers have been shown to publish less often in international journals then do researchers from Malaysia, Thailand and Singapore.[18] No wonder, the absolute publication rate for Indonesian research is lower compared to other Asian countries.[19] This may be explained by the lack of research funding as well as the lack of English proficiency and writing habit among Indonesian researchers.[20]

Systematic reviews of the effectiveness of health care interventions are placed on the top in the hierarchy of evidence. We only found three of these among the articles we had reviewed. In particular in a healthcare community with limited resources, like Indonesia, systematic reviews and economic evaluation studies are a valuable source for clinicians and policy-makers. Still, they are not well-known in the Indonesian health care community. This may have been caused by the limited access to medical literature and limited skills of Indonesian researchers on systematic reviews.

Quality comparison of the medical publications –Compared to other medical fields an overall 15% high quality studies can be considered acceptable, i.e. 10% of the publications in physical therapy and 24% in ophthalmology can be considered as high quality.[14, 21]

The proportion of high quality PubMed indexed studies is twofold than non-PubMed indexed. This might be explained by the fact that among the eight non-PubMed indexed Indonesian journals that were included, none of them endorsed the use of international reporting guidelines included in the Equator Network Library.[22] Three percent Chinese and 33% Indian high impact medical journals endorsed the Consolidated Standards for the Reporting of Trials (CONSORT) statement.[7, 9]

The main concern in all study types, and in particular "therapy" studies, was the lack of reporting on blinding. This seems to be overlooked by the researchers, the Indonesian reviewers and editors. For "therapy" studies only 39% in PubMed indexed journals and 15% in non-PubMed indexed journals reported blinding. A previous study among a sample of placebo-controlled trials published in PubMed from 1985 to 1997 reported blinding for 80% of 60 studies.[23] However, 33% of 196 trials in rheumatoid arthritis and 38% of 68 trials in dermatology also fail to state whether blinding was used.[24] Also evaluation on the quality of reporting of diagnostic accuracy studies showed that only relatively few articles (37% of the 124) reported blinding.[25] Blinding is particularly important when outcome measures involve some subjectivity. When it is not possible to blind the clinicians or patients, blinding of the outcomes observers does needs to be ensured to reduce risk of information bias.[26]

While random and concealed treatment allocation reduces the risk of selection bias especially in "therapy" studies[26] only about half of the "therapy" studies reported on random allocation or further specified the methods of sequence generation. Moreover, in only 20% this criterion was satisfied. It is of course disappointing, since trials based on non-random methods generally yield bias in estimating treatment effects.[(24)]

Improving the quality of reporting of research papers could be endorsed by implementing the international standardized reporting guidelines in Indonesian journals. Since the scientific value of biomedical journals relies on the peer review process and on editorial decisions, it is reasonable to recommend that the peer review process incorporated a strategy to ensure adherence to the reporting guidelines. Yet, one study proved that this approach did not improve the quality of the manuscript as high as expected since authors have difficulties in adhering to high standards of reporting during the writing phase.[27] Awareness of the reporting guidelines should be guaranteed during the design and execution of the study.

Conclusion

A relatively small proportion of studies by Indonesian researchers met the international standards for quality reporting or methods. Continuous effort to improve the availability and quality of the research evidence in Indonesia and similar countries in Asia Pacific should be done simultaneously with dissemination of EBP skills among health professions.

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Chapter 6

From West to East; experience with adapting a curriculum in Evidence-based Medicine

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Abstract

Background - *Clinical Epidemiology (CE) and Evidence-based Medicine (EBM) have become an important part of medical school curricula. This report describes the implementation and some preliminary outcomes of an integrated CE and EBM module in the Faculty of Medicine Universitas Indonesia (UI), Jakarta and in the University of Malaya (UM) in Kuala Lumpur.*

Methods - *A CE and EBM module, originally developed at the University Medical Center Utrecht (UMCU), was adapted for implementation in Jakarta and Kuala Lumpur. Before the start of the module, UI and UM staff followed a training of teachers (TOT). Student competencies were assessed through pre and post multiple-choice knowledge tests, an oral and written structured evidence summary (evidence-based case report, EBCR) as well as a written exam. All students also filled in a module evaluation questionnaire.*

Results - *The TOT was well received by staff in Jakarta and Kuala Lumpur and after adaptation the CE and EBM modules were integrated in both medical schools. The pre-test results of UI and UM were significantly lower than those of UMCU students ($p<0.001$). The post-test results of UMCU students were comparable ($p=0.48$) with UI, but significantly different ($p<0.001$) from UM. Common problems for the modules in both UI and UM were limited access to literature and variability of the tutors' skills.*

Conclusions - *Adoption and integration of an existing Western CE-EBM teaching module into Asian medical curricula is feasible while learning outcomes obtained are quite similar.*

Background

To be able to provide 'best practices', all health care professionals should be able to practice Evidence-based Medicine (EBM). This requires that medical decisions are based on the best available, current, valid and relevant evidence. In order to do that, medical graduates should 'be able to gain, assess, apply and integrate new knowledge and have the ability to adapt to changing circumstances throughout their professional life'.[1, 2] Nowadays many medical schools around the world have incorporated EBM teaching program into their curriculum.[3] However, reports on EBM teaching for undergraduate medical students in Asian countries are limited.[4-8]

The Sicily statement on teaching Evidence-based Practice recommends to incorporate knowledge, skills and attitudes of EBM into medical training.[1] However, developing a new curriculum is a challenging task which draws heavily on resources. An alternative is to adopt established EBM and Clinical Epidemiology (CE) modules and adapt these before implementing them in the existing curriculum.

The AsiaLink Clinical Epidemiology and Evidence-based Medicine (CE-EBM)[9] aims to improve the level of knowledge and skills in CE and EBM of medical students, medical doctors, clinical researchers and other health care professionals in Indonesia and Malaysia. The activities include incorporating CE and EBM teaching in the undergraduate medical curriculum in both the University of Indonesia (UI) and the University of Malaya (UM).

Currently, little is known about the effects of the 'adapt to adopt' approach used in curriculum adaptation with regard to EBM and CE teaching. Many papers on EBM and CE teaching report comparisons of different methods of teaching, usually within one medical school. This report describes the process of adapting the existing Utrecht CE and EBM modules and the implementation in an Indonesian and Malaysian curriculum and reports

some preliminary outcomes in three medical schools (UI, UM and UMCU). It is also aims to illustrate how some challenges and differences were addressed during the implementation.

Methods

The Clinical Epidemiology and Evidence-based Medicine (CE-EBM) module

The University Medical Centre Utrecht revised its medical school curriculum in 1999. This involved development of a clinical epidemiology (CE) module and an Evidence-based Medicine (EBM) module. The Utrecht CE module is a six-week full-time module targeted to third-year students, which is also the year of their first clinical rotation. The Utrecht EBM module is a six-week part-time module for sixth (final) year students. During that sixth year, students also have their clerkship. Table 1 presents the content and aim of the Utrecht's CE and EBM modules.

Medical training in the three medical schools differs. At UMCU it comprises a 3-year preclinical Bachelor's and a 3-year clinical Master's program; at UI it takes 3 preclinical years and 2 clinical years; at UM it takes 2 preclinical years and 3 clinical years of training. Therefore, it was not possible to copy and implement the UMCU modules. It was decided to merge and integrate the Utrecht CE and EBM modules. The new module was developed through intensive discussion between the coordinators of the CE and EBM modules of UMCU, UI and UM. It was decided to translate all teaching materials (originally in Dutch) into English. A native speaker assisted this translation and checked the final versions. At UM, English was already the language of teaching but not at UI. Still, it was decided to familiarize the Indonesian students with English as the most-used language in medical literature.

In UMCU both the CE module and EBM modules were coordinated by the clinical epidemiology division of the Julius Center of the Health Sciences

and Primary Care, who have approximately eight years of experience in teaching this module. Clinicians from various departments are also involved as tutors in group work. In UI, the lecturers are clinicians or non-clinicians who have formal training in clinical epidemiology or EBM. Some have more than five years' experience in conducting EBM courses while the tutors are clinicians who have participated in the CE or EBM course. In UM, the lecturers are staff of the Social and Preventive Medicine Department who are experienced in teaching epidemiology and biostatistics. The tutors are also clinicians; however some have never participated in CE or EBM courses.

Table 1. Content of the Clinical Epidemiology and Evidence-based Medicine (CE-EBM) module

Topic	Methods	Module*
Introduction to Evidence-based Medicine	Lecture	EBM
How to make an evidence-based case report	Lecture	EBM
Making an answerable clinical question	Lecture	EBM
Frequency and association measures	Lecture	CE
Diagnosis	Lecture	CE
Prognosis	Lecture	CE
Formulation of the clinical question; search and comparison of study-book knowledge, study of EBCR design	Group work	EBM
Intervention	Lecture	CE
Etiology	Lecture	CE
Critical appraisals	Lecture	EBM
Internet literature search	Practical lecture	EBM
Computer exercise on prognosis and diagnosis	Practical lecture	CE
Exercise critical appraisal on therapy	Group work	EBM
Establishing the search query, literature search and selection, critical appraisal of the selected papers regarding their relevance and methods, description of methods and (provisional) results.	Group work	EBM
Levels of evidence	Lecture	EBM
Computer exercise on aetiology and intervention	Practical lecture	CE
Exercise critical appraisal on prognosis and diagnosis	Group work	EBM
Sorting and structurally summarize the search and appraisal; description of methods and (provisional) results.	Group work	EBM
Exercise critical appraisal on aetiology	Group work	EBM
Report of EBCR both orally and in writing according to the requirements for form, structure and content; formulation of a recommendation for patient care and further research.	Group work	EBM

*based on the original structure in UMCU where the CE and EBM were given in separate module.

Before, during and after implementation of the module, personal teaching experiences and evaluation results were shared and discussed, both in an informal and a formal manner. First of all, to familiarize the local staff later involved in teaching the module, a training of teachers (TOT) in UI and UM was led by two experienced lecturers and the module developers from UMCU. This TOT was conducted for three days and consisted of lectures and computer practice. In addition, there were regular formal discussion meetings between teachers teams (lecturers, tutors and coordinators) within each university and between the module coordinators of UI (ISW), UMCU (GvdH) and UM (MFM). At the end of each meeting, action points for implementation and optimization of the modules were articulated whenever necessary.

The CE-EBM module in UI was given as a four-week module (condensed) at the end of their fourth year. In UM, it was conducted dispersed within the three-month period of the Social and Preventive Medicine (SPM) module for third-year medical students. The time allocated for the CE-EBM within the SPM module is a three-hour session twice a week. Moreover, the SPM module is held in a remote satellite campus. Before attending the CE-EBM module, students have passed a research module (UI) or epidemiology and biostatistics module (UM). The comparison of the CE-EBM module structure in the three medical schools is presented in table 2.

A series of lectures on the diagnostic, prognostic, therapeutic (intervention), and etiological research were given to re-orientate students on the research design methods relevant to the CE-EBM module. These were further reinforced through computer practice. Lectures introduced students to EBM and the specific skills needed; notably, attention was also given to formulating clinical questions and searching the literature. Critical appraisal skills for relevance and risks of bias and summarizing evidence were taught in small working groups.

Table 2. Comparison of the CE-EBM module structure in UI, UM and UMCU

Educational activities within the module	Time allocation (hours)			
	UI	UM	UMCU	
			CE	EBM
Lectures	30	22	20	20
Computer practical	6	8	10	3
Tutorial working group	18	14	5	8
Collaborative and individual learning*	45	0	110	55
Plenary presentation	4x3	2x3	4x3	4x3
Total hours	111	50	157	98
Module duration	4 week	3 months	6 weeks	5 weeks

* Specifically allocated within the module as listed in the schedule

The final task of the students was to develop an Evidence-based Case Report (EBCR). An EBCR summarizes the best available evidence and translates it into practice. It follows an explicit and transparent approach to identify such evidence and thereby can help resolve a dilemma in decision-making in real-life patient management. It can be applied at all stages of patient care, notably diagnosis, prognosis and treatment.[10, 11]

Students developed their EBCR based on a real clinical patient scenario they had encountered during a previous clinical rotation in tutor-supervised small student groups (n=5). Once a week (in UI and UMCU), the progress in EBCR development was reported in a plenary presentation. These plenary presentation sessions were moderated by experts in clinical epidemiology and EBM, who provided students with feedback. Through these plenary presentations, students were able to learn about different clinical problems of other groups and the appropriate method(s) of dealing them. Due to constraints of the existing curriculum at UM, the plenary presentations were conducted twice during the three-month module: the first to report the clinical question and the second to report the final EBCR.

Student assessment

As formative evaluation, students completed a pre- and post-module knowledge test. This test consisted of 32 multiple-choice questions (MCQ) regarding concepts of etiological, diagnostic, prognostic, therapeutic research and frequency measures. Most of the questions have yes or no answering options, some have five options. In UMCU, this test is used to evaluate the CE module.

EBCRs were assessed using a standard scoring form. The form was based on principles of explicit and transparent reporting of evidence summaries, and included: question, information search, study assessment, data extraction, data synthesis, conclusion, and discussion. The EBCR grades, on a scale of 1 to 5 (insufficient, doubtful, sufficient, good or excellent), were based on the overall impression of assessors. A student passed the EBCR assignment with a score equal to or above 3 (sufficient, good and excellent). Ratings for the above separate criteria were also provided as feedback on the aspects that could be improved, with a comment for three categories with the lowest ratings and the highest ratings. The overall scores were multiplied by 2 to comply with the standard 10-point rating scale used at UI and UM. At UMCU and UI the EBCRs were rated by tutors of working groups, while at UM this was done by the module coordinator.

At the end of the CE module at UMCU and the CE-EBM module at UI and UM a summative evaluation was taken by asking the students to assess the quality of one research article. Students completed a module evaluation questionnaire including questions on the quality of teachers, content and organization of the module.

Analysis of student assessment data

The knowledge test score was converted into a 1 to 100 score by computing the percentage of correct answers assuming that all questions have similar weight. The scores between universities were compared using an independent t-test. ANCOVA was performed to compare the knowledge test score before and after the module, with control for differences in the pre-test results. All analyses were performed using the SPSS 11.0 (SPSS Inc., Chicago, IL).

Ethical considerations

The CE-EBM module implemented in UI and UM was to become part of the medical curriculum and the effect assessment became part of module evaluation which should be undertaken by all the students. As such, the managerial considerations on the curriculum revision dominated over possible ethical considerations. However, all data were analyzed and reported anonymously.

Results

We evaluated the results of the module implementation in 2010. In UI, the CE-EBM module was conducted from May to July in two rotations with a total of 202 students. In UM, the module was implemented from September until December 2010 for 200 students. The EBM module in UMCU was conducted throughout the year, divided into six groups; a total of 381 students participated.

Table 3. Comparison of pre and post-knowledge test results and Evidence-based Case Report (EBCR) score between UI, UM and UMCU

		UMCU	UI	UM
Pre-test scores	n	389	196	160
	Mean (SD)	62.20 (9.21)	54.69 (10.51)	46.23 (8.69)
	Minimum	9.38	31.58	28.12
	Maximum	87.50	92.11	68.75
Mean difference (95% CI)			7.52 (5.85-9.18)	15.97 (14.30-17.64)
p-value			<0.001*	<0.001*
Post-test scores	n	377	196	200
	Mean (SD)	74.75 (9.66)	73.54 (10.13)	61.39 (10.39)
	Minimum	31.25	34.21	18.75
	Maximum	100	89.48	81.25
Mean difference (95% CI)			1.32 (0.40-3.04)	13.36 (11.66-15.06)
p-value			0.484†	<0.001†
Difference in scores	n	350	196	159
Post-test minus pre-test		12.54 (11.44)	18.85 (12.81)	17.51 (9.49)
Mean difference (95% CI)			6.32 (4.22-8.41)	4.98 (2.93-7.02)
p-value			<0.001*	<0.001*
EBCR	n	71	40	40
	Median	8.0	8.4	7.8
	Minimum	5	7.5	7
	Maximum	10	9.0	8.6
p-value			0.001‡	0.44‡

*Independent t-test
†Ancova test, which include baseline score as covariate.
‡Mann-whitney test

Student assessment

Table 3 shows the results of the pre- and post-module knowledge assessment and EBCR scores at UI, UM and UMCU. The mean pre-test results of the UI students were significantly lower than those of the UMCU ($p<0.001$). After the module, the improvement (change) of knowledge in UI students was significantly higher than for the UMCU students ($p<0.001$), which resulted in comparable post-test results ($p=0.484$). On the other hand in the UM, even though the improvement (change) of knowledge of the students was also significantly higher than at UMCU ($p<0.001$), the post-test results were still significantly lower than for the UMCU ($p<0.001$). The mean EBCR score of UI students was significantly higher ($p=0.001$) compared with both UMCU and UM. Examples of some of the clinical problems answered by EBCR are presented in Table 4.

Table 4. Examples of clinical questions answered by the Evidence-based Case Reports

Clinical questions	Type of question
University of Indonesia	
Is arthemeter-lumefantrine (AL) as effective as artesunate amodiaquin (ASAD; standard treatment of malaria therapy in Indonesia) for treating uncomplicated childhood malaria?	Therapy
Mortality after balloon aortic valvuloplasty in male with severe aortic stenosis	Prognosis
Is the nitrite test accurate as diagnostic tool in pregnant women?	Diagnosis
In hospitalized elderly patients, is depression related to higher mortality?	Prognosis
Could calcium supplementation prevent osteoporotic fracture in post-menopausal women?	Therapy
Diagnostic value of abdominal radiography to diagnose acute appendicitis in children.	Diagnosis
The effectiveness of normal saline solution vs Ringer's lactate solution to overcome dengue shock syndrome in children	Therapy
Is acupuncture effective to decrease pain in patient with chronic back pain?	Therapy
University of Malaya	
Is exercise stress echocardiography superior in diagnosing patients presenting with chest pain compared with exercise stress electrocardiography?	Diagnosis
Can Parkinson's disease be treated more effectively by using dopamine agonists compared with levodopa in Parkinson patients above 50 years?	Therapy
Do colorectal cancer patients with high levels of tumor markers CEA and CA19-9 have a low 3-year survival rate?	Prognosis
Does the Revised Trauma Score (RTS) make a good prognostic tool in trauma patients?	Prognosis
Do children with past history of sexual abuse have increased risk of psychiatric problems in adulthood?	Prognosis
University Medical Center Utrecht	
The prognostic value of a history of shoulder pain on predicting the duration of pain in patients presenting with a new episode of shoulder pain.	Prognosis
The influence of physiotherapy on pain in patients with shoulder impingement.	Therapy
Diagnostic ultrasound in a patient suspected of a partial rotator cuff rupture.	Diagnosis
Does treatment with heparin in adults diagnosed with cerebral venous thrombosis reduce mortality within 3-months?	Therapy
CT venography: the new reference test for diagnosing cerebral venous thrombosis?	Diagnosis
Glasgow Coma Scale as a prognostic factor in sinus thrombosis.	Prognosis
Prognostic value of current smoking for exacerbations in COPD.	Prognosis
For patients with COPD in the primary care setting: what is the predictive value of CRP for community-acquired pneumonia?	Prognosis
Diagnostic value of BNP for determining chronic heart failure in patients with COPD.	Diagnosis

Module evaluation

The three medical schools have a different module evaluation format, thus no statistical testing was performed to compare the results. In general, more than 80% of students in UI and UMCU agreed that the module increased their knowledge and skills as shown in Table 5. Students especially appreciated the searching and critical appraisal skills they learnt through this module which they believed to be very useful for their future.

Only 49% of UM students agreed that this module had achieved its objectives as compared with 89% in UI. Several problems were mentioned by students in the module evaluation as well as reported by module coordinators in both UI and UM including limited access to literature (UI), inconsistent internet connection as students were located in a remote satellite campus (UM) and the variability of the tutors' skills despite the TOT (UI and UM). To help the students retrieve some articles which are not accessible through the current library access at UI, tutors or module coordinators sometimes needed to contact their colleagues in other institutions with better library access (both inside and outside the country) who could provide the articles. The variability in tutors' skills was handled by providing adequate time for discussion among tutors and resource persons during the module through regular meetings and electronic communication. Besides that, both UI and UM students thought that the searching skills should have been introduced earlier.

Table 5. Module evaluation by students at the end of the module.

	Proportion of students agree (%)		
	UI	UMCU	UM
The objective of the course is achieved	89	N.A	48.7
The course increased my competence (knowledge and skills)	85	95	N.A
The course is useful for my professionalism	N.A	60	56

Discussion

This report shows that implementation of an adopted CE-EBM curriculum from a Western country (the Netherlands) in Eastern countries (Indonesia and Malaysia) resulted in a comparable increase in medical student knowledge. The introduction of a CE-EBM module as part of the medical curriculum is needed as a response to global development. Adaptation of an established module was chosen as a more practical approach instead of developing a new one. Yet, it still has its own challenges. A modification process which comprises broad aspects such as learning objectives, resources, institutional mandates and values needs to be carried out to provide more context.[12]

A survey about EBM teaching in UK medical schools has identified similar challenges including the need for standard curriculum and teaching materials, the lack of people trained in EBM to facilitate small group sessions, and also the need for an identifiable coordinator who is responsible for the development and integration of EBM into the medical school curriculum.[13] Our experience shows that those challenges could be minimized using this 'adapt to adopt' approach.

Learning goals

EBM is defined as the uptake and use of best available evidence, and its integration with clinical expertise and patients' values, in circumstances of individualized patient care. The underlying assumption in the definition of EBM is that all aspects on the principles, knowledge and skills needed for this are mastered. The modules used at UMCU, UI and UM are based on the principles of information mastery included in the Sicily statement on teaching Evidence-based Practice.[1] In the context of self-directed and problem-based learning this implies that we aim for the third level of Miller's pyramid.[14]

Student assessments

To determine the effect of a curriculum intervention, a prospective pre-test-post-test controlled trial is the strongest study design.[12] The results of knowledge tests during the CE module at the UMCU and the CE-EBM module test at UI and UM were compared. Despite the research module (UI) and epidemiology and biostatistics module (UM) attended prior to the CE-EBM module, the scores of the UI and UM students during pre-test were significantly lower compared with those of UMCU students. It seems that both previous modules at UI and UM focused more on the study design (i.e. cross-sectional, case-control, cohort and experiment) and bio-statistics rather than the clinical epidemiology approach (diagnostic, prognostic, therapeutic and etiological).

A standard scoring form was used for EBCR assessment, but there was no training or standardization of these assessments. Differences in the EBCR ratings may be explained by different raters and variation among them. While at UM there was only one rater, the Jakarta tutors may - compared with the UMCU raters - have been too unfamiliar to this kind of report. This may in part explain the negatively skewed distribution of EBCR ratings at UI.

Students knew that the MCQ test scores served as a formative evaluation, so these were not included in the module grading. We did not apply correction for guessing for the MCQ test. Since all questions were to be completed and no answers could be left blank, guessing might result in both higher or lower scores.[18] Still, an increase in MCQ score was observed.

The knowledge test was developed based on the predefined module learning goals, and thus determined the content and face validity of the test as educational measurement tool. The test outcomes presented may, however, represent a mix of results based on the quality of the module,[15] teachers[16]

and students[17]. A formal psychometric evaluation of the reliability has not yet been performed.

Although a formal psychometric evaluation of the student assessment tests may deepen insight into their quality and may perhaps provide a more detailed view on the reported differences between UMCU, UI and UM in learning outcomes, it is not the purpose of our paper to show the quality of the tests used. But given the content and face validity of the tests used we consider these appropriate to illustrate the success of the adoption of the CE-EBM module at UI and UM medical schools.

Schools compared

Despite a lot of differences between the three medical schools, the post-module results show that similar effects were achieved on students' knowledge and skills in UI and UMCU. In design and organization the UI module more closely resembled the original Utrecht teaching modules. The full-time 4-week CE-EBM module in year 4 at UI resulted in comparable score with UMCU, which ran a separate full-time 5-week CE module in year 3 and a 5-week part-time EBM module in year 6.

Due to cultural differences in the approach to teaching and learning and in health care systems, it was expected that the use of Western teaching material and approach in Asian context and environment may pose particular challenges. This may have played a role in the success of this curriculum revision at UM and UI. Indonesia and Malaysia are still considered to be developing countries. Several obstacles to teaching and practicing EBM in the developing world have been identified, including limited resources, limited access to databases and libraries, and lack of role models.[8] Those factors need to be considered during the process of adapting the curriculum from a Western developed country (the Netherlands) to UI and UM. Still, since 2012 the module has proved to be a success at both UI and UM and is still in place.

From the start, the UM module had a more complex environmental and organizational structure. The differences in the module implementation were probably too abundant in UM thus similar results were not being observed. This is also corroborated with the result of the module evaluation which showed that a great number of the UM students felt that this module failed to achieve its objectives. Moreover, students and teachers at UI and UM were quite used to a problem-based learning (PBL) or a self-directed learning approach. For teaching EBM, however, directed learning including lectures followed by a group tutorial may be more effective than PBL.[6]

Study limitations

Systematic differences in the structure, time, approach of the module and a difference in their place in the curricula of the three medical schools could not be controlled for. Some differences in the tools used for student assessments (i.e. module evaluation questionnaire, EBCR ratings) may have had an impact on our findings. Despite these limitations, the measured objective and standardized outcomes in the large number of participating students in a multi-institutional comparison contribute to the robustness of the findings of our study.[19]

Conclusions

Adoption of an existing Western EBM module into Asian medical curriculums is feasible and more practical than developing a new one. Despite differences in the program and the students, similar learning goals can be reached in different ways. Our experience could be used by other medical schools in Asian countries to start teaching EBM to their medical students.

Declaration of interests

The authors report no declarations of interest. The authors alone are responsible for the content and writing of the article.

Authors' contributions

ISW wrote the original draft. GvdH, MFM, YvdG, AB and SS contributed to the concept and all revised drafts of the report.

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Chapter 7

Direct short-term effects of EBP teaching: change in knowledge, not in attitude; a cross-cultural comparison among students from European and Asian medical schools

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Abstract

Background *- We report about the direct short term effects of a Clinical Epidemiology and Evidence-based Medicine (CE-EBM) module on the knowledge, attitude and behavior of students in the University Medical Center Utrecht (UMCU), Universitas Indonesia (UI) and University of Malaya (UM).*

Methods *- We used an adapted version of a 26-item validated questionnaire, including 4 subscales: knowledge, attitude, behavior and future use of Evidence-based Practice (EBP). The 4 components were compared among the students in the three medical schools before the module using one-way ANOVA. At the end of the module we measured only knowledge and attitudes. We computed Cronbach's alpha to assess its validity in our population. To assess the change in knowledge and attitudes we used the paired T-test in the comparison of scores before and after the module.*

Results *- In total 526 students (224 UI, 202 UM and 100 UMCU) completed the questionnaires. In the 3 medical schools Cronbach's alpha for the pre-module total score and the 4 subscales scores always exceeded 0.62. UMCU students achieved the highest pre-module scores in all subscales compared to UI and UM with the comparison of average (SD) score as the following: knowledge 5.04(0.4) vs 4.73(0.69) and 4.24(0.74); [p<0.001], attitude 4.52(0.64) vs 3.85(0.68) and 3.55(0.63); [p<0.001], behavior 2.62(0.55) vs 2.35(0.71) and 2.39(0.92); [p=0.016], and future use of EBP 4.32(0.59) vs 4.08(0.62) and 3.7(0.71); [p<0.01]. The CE-EBM module significantly increased the knowledge of the UMCU (from average 5.04+0.4 to 5.35+0.51; p<0.001) and UM students (from average 4.24+0.74 to 4.53+0.72; p<0.001) but not UI. The post-module scores for attitude did not change in the three medical schools.*

Conclusion *- EBP teaching had direct short term effects on knowledge, not in attitude. Differences in pre-module scores are most likely related to differences in the system and infrastructure of both medical schools and their curriculum.*

Introduction

Evidence-based Practice (EBP) is being considered as an essential component of training in the health professions.[1] An increasing number of medical schools around the world have incorporated EBP teaching in their curricula.[2] As such, establishing an EBP module involves ”a planned educational experience that encompasses behavioral goals, instructional methods, and the actual experience of the learners”.[3] Learning goals encompass three components: knowledge, skills and attitudes.[1] Changes in attitudes and perceptions as well as knowledge are important precursors to changes in behavior.[2] In spite of the need, incorporation of teaching in EBP in an existing curriculum is for some medical schools a challenging task, especially those with limited resources as in developing countries. The alternative approach is to adapt an establish one.

An existing Clinical Epidemiology and Evidence-based Medicine (CE-EBM) module originating from a European country (University Medical Center Utrecht (UMCU), the Netherlands) has been adopted and implemented in two Asian countries (Universitas Indonesia (UI) and University of Malaya (UM)). The learning goals of this module aim to produce doctors who are able to practice all five steps of EBP (asking, acquiring, appraising, applying, assessing) or an EBP ‘doers’ as defined by Straus et al.[4] Our experience shows that Evidence-based Medicine (EBM) curriculum is feasible.[5]

As this CE-EBP module is a new part of the curriculum in both medical schools (University of Indonesia and University of Malaya), there is a need for a comprehensive evaluation of learning effects. The initial quality evaluations showed that the module was well received by the medical students and their teachers. In general the students’ knowledge increased, learning goals of the module have been achieved, while students indicated to learn much.[5] These were achieved despite differences in the medical

education structure, schools' curriculum, health care system, as well as culture of the communities.

This report aims to study (a) the direct short term effects of the EBM module on the knowledge and attitude of the students in UMCU, UI and UM, and (b) compare the knowledge, attitude and behavior of students in UMCU, UI and UM.

Methods

EBM module

The content and structure of the EBM module implemented in the three medical schools has been described elsewhere.[5] The module was implemented first in the UMCU before it was adapted and adopted by UI and UM. In short it follows the principles of the Sicily statement on EBM teaching[1] and includes lectures on the design and conduct of diagnostic, therapeutic, prognostic and etiologic studies, computer practices on literature search and data analysis, tutored group discussions on EBM assignments and moderated plenary assignment presentations. Small groups of 5 students are assigned to develop an Evidence-based Case Report (EBCR), i.e. comprehensive best evidence summary for information needs from patient care.[6] Students submit their EBCR in written form and as oral presentations at the end of the module. Students are evaluated and marked for their EBCRs, a written exam, and for their activity during small group discussions.

To fit the local situations, the module is implemented differently. In UMCU, the CE and EBM modules are run separately as a six-week full time CE module targeted to 3rd year students and a six-week part-time EBM module for 6th (final) year students. In UI and UM, both modules were merged in to an integrated CE-EBM module. The CE-EBM module in UI was given to the medical students as a four-week module (condensed) at the end of their 4th year. In UM, it was conducted dispersed within the three months period

of Social and Preventive Medicine (SPM) module for 3rd year medical students.

Instrument selection

In finding the most suitable instrument for our purposes we chose a questionnaire assessing knowledge, attitude and behavior (KAB) which has been developed by a team from the University of Hong Kong.[7] This questionnaire is mentioned in the Sicily statement,[1] and is considered relevant for evaluation of EBM teaching and has been thoroughly validated[7]. The questionnaire contains 26 items which is classified in to four subscales: knowledge (5 items), attitudes (6 items), application (6 items) and future use (9 items). Students were asked to mark each item on a 6-point Likert or adjectival scale (strongly agree – strongly disagree, not at all – completely, never – all the time, very difficult – very easy, completely useless – very useful, very unwilling – very wiling). With Cronbach's alphas of the whole questionnaire and of each subscale exceeding 0.7, the internal consistency has been shown to be satisfactory.[7, 8]

Instrument adaption

The questionnaire was originally in English and no translation to local languages (Indonesian, Malay or Dutch) was considered necessary. Based on the assessment of the fit of the items for the local situation and purposes, almost all of the questions were considered as highly relevant. However, modification was implemented to four of the attitude questions which asked the students to compare their present attitude with that one year ago. As we thought that the statements may confuse the students, we decided to only ask the respondent to score according to their present condition.

Data collection

The questionnaire was completed by students enrolled in the CE-EBM module in the three medical schools. The questionnaire was administered

twice: at the beginning of the module and at the end. At the start of the module the complete 26-item questionnaire was completed. We did not expect changes in behavior in the short term, immediately at the end of the module. Therefore, at the end of the module, only the 11 items of the knowledge and attitude subscales were to be completed.

Instrument consistency

To assess the internal consistency of the adapted questionnaire Cronbach's alpha was computed separately for each school. The subscale scores were obtained by calculating the mean score of all the items in each subscale. One-way ANOVA was used to compare the knowledge, attitude, behavior and future use of EBP among students in the three medical schools at the start of the module. The effect of the EBM module on the knowledge and attitude of the medical students in each school was assessed by comparing the score before and after the module using the paired t-test. All analyses were performed using SPSS Version 11.0 (SPSS Inc., Chicago, IL).

Ethical consideration

The CE-EBM module implemented in UI and UM was to become part of the medical curriculum and the effect assessment became part of module evaluation which should be undertaken by all the students. As such, the managerial considerations on the curriculum revision dominated over possible ethical considerations. However, all data were analyzed and reported anonymously.

Results

The questionnaire was implemented in 2010 in the University of Indonesia (UI) and University of Malaya (UM) and 2010-2011 in University Medical Center Utrecht (UMCU). In total 526 students completed the questionnaires,

all in the clinical stage of their curriculum: 100 students from UMCU in their 6th year, 224 students from UI in their 4th year, 202 students from UM in their 3rd year participated. The questionnaires completed before the start of the module at the three medical schools showed that Cronbach's alpha exceeded 0.74 for the total questionnaire, and exceeded 0.62 for all 4 subscales (Table 1).

Table 1. Analysis of internal validity (Cronbach's alpha) of the questionnaire on the Evidence-based Practice knowledge, attitude, behavior and future use, in the Universitas Indonesia (UI), University of Malaya (UM) and University Medical Center Utrecht (UMCU).

Components	**UMCU (n=100)**	**UI (n=224)**	**UM (n=202)**
EBP knowledge	0.745	0.862	0.854
Attitudes toward EBP	0.688	0.765	0.626
Personal application and use (behavior) of EBP	0.677	0.757	0.754
Future use of EBP	0.833	0.814	0.841

The pre-module scores in the three medical schools are presented in Table 2. Overall, significant differences were observed in the students' knowledge, attitude, application and future use of EBP in the three medical schools. Compared to students from UI and UM, those at UMCU achieved highest pre-module scores in all subscales. The average(SD) score of UMCU students compare to UI and UM in knowledge are 5.04(0.4) vs 4.73(0.69) and 4.24(0.74); [p ANOVA<0.001]. Average(SD) attitude score 4.52(0.64) vs 3.85(0.68) and 3.55(0.63); [p ANOVA<0.001]. Average(SD) behavior score 2.62(0.55) vs 2.35(0.71) and 2.39(0.92); [p ANOVA=0.016]. Average(SD) future use of EBP score 4.32(0.59) vs 4.08(0.62) and 3.7(0.71); [p ANOVA<0.001]).

Table 2. Comparison of scores for subscales for knowledge, attitudes, application and future use of Evidence-based Practice (EBP), prior to the EBP-modules in the Universitas Indonesia (UI), University of Malaya (UM) and University Medical Center Utrecht (UMCU).

Factors	Mean score (SD)			p
	UMCU (n=100)	UI (n=224)	UM (n=202)	
EBP knowledge	5.04 (0.40)	4.73 (0.69)	4.24 (0.74)	<0.001 (overall) <0.001 (UI vs UMCU) <0.001 (UM vs UMCU) <0.001 (UI vs UM)
Attitudes toward EBP	4.52 (0.64)	3.85 (0.68)	3.55 (0.63)	<0.001 (overall) <0.001 (UI vs UMCU) <0.001 (UM vs UMCU) <0.001 (UI vs UM)
Personal application and use (behavior) of EBP	2.62 (0.55)	2.35 (0.71)	2.39 (0.92)	0.016 (overall) 0.016 (UI vs UMCU) 0.048 (UM vs UMCU) 1.00 (UI vs UM)
Future use of EBP	4.32 (0.59)	4.08 (0.62)	3.70 (0.71)	<0.001 (overall) 0.006 (UI vs UMCU) <0.001 (UM vs UMCU) <0.001 (UI vs UM)

Knowledge, attitude, application and future use were measured by 6-point Likert scale questions. The score for each factor was obtained by calculating the mean score of all the items in each respective factor.

p-values were obtained using One Way ANOVA test with post hoc analysis accounting for school.

Table 3 displays the post-module knowledge and attitude scores for the knowledge and attitude subscales. The three medical schools differ and the UMCU students reached significantly higher scores compared to UI and UM in knowledge (average[SD] of 5.35[0.51] vs 4.73[0.75] and 4.53[0.72]; p of ANOVA <0.001) and in attitude, (average[SD] of 4.42[0.58] vs 3.83[0.85] and 3.58[0.72]; p of ANOVA <0.001). The post module scores of the knowledge subscale were significantly increased (p of paired t-test <0.001) in UMCU (from average[SD] of 5.04[0.4] to 5.35[0.51]) and UM (average[SD] of 4.24[0.74] to 4.53[0.72]), but not in UI students. The post-module scores for the attitude subscale did not change in the three medical schools (p of paired t-test >0.1).

Table 3. Change of scores for subscales for knowledge, attitudes, application and future use of Evidence-based Practice (EBP), prior to the EBP modules in Universitas Indonesia (UI), University of Malaya (UM) and University Medical Center Utrecht (UMCU).

Factors	Mean score (SD)		p
	pre	post	
EBP knowledge			
UMCU	5.04 (0.40)	5.35 (0.51)	<0.001
UI	4.73 (0.69)	4.73 (0.75)	0.096
UM	4.24 (0.74)	4.53 (0.72)	<0.001
Attitudes toward EBP			
UMCU	4.52 (0.64)	4.42 (0.58)	0.136
UI	3.85 (0.68)	3.83 (0.85)	0.586
UM	3.55 (0.63)	3.58 (0.72)	0.470

Knowledge, attitude, application and future use were measured by 6-point Likert scale questions. The score for each factor was obtained by calculating the mean score of all the items in each respective factor.

p-values were obtained using paired t-test.

Discussion

Our data on our cross cultural comparison of the short term effects of EBM teaching in three different medical schools in Asia and Europe shows direct changes in knowledge. Due to the short follow-up, changes in attitude and behavior remain to be shown.

Questionnaire consistency

To be able to compare the impact of an EBP teaching in three different schools, a validated instrument is needed which corresponds with the objectives and learning goals of the curriculum. Among 104 unique EBP assessment tools identified in one systematic review; only a few of the instruments included in that review evaluate the attitude while none met the pre-determined validity criteria.[13] This KAB questionnaire was selected because it measures several components at once. It has been developed and is already implemented in

Asian medical schools. The questionnaire was developed through a 4-step approach to confirm that the questionnaire has adequate face, content, criterion and construct validity[7, 12]. Johnston et al.[7] found that the Cronbach's alpha values of each component in the original questionnaire ranged from 0.71 to 0.88. As we slightly adapted the questionnaire, we repeated the analysis for the internal consistency of the questionnaire. In this study we observed Cronbach's alpha in the same range.

Limitations of study

This study has several limitations which may complicate the interpretation of findings. Firstly, the maintenance of the English as the original language of the questionnaire which could cause difficulties in some students especially those from Indonesia and Netherlands. The second limitation is differences in some base line characteristics such as the year of the medical students and previous exposure to Evidence-based Medicine due to differences in curriculum structure as well as cultural and environmental aspects in each country. Cultural and linguistic differences as well as characteristics differences might cause bias on the results due to potential differences in the perception and interpretation of terms.[14, 15] Thirdly, this questionnaire measured self-reported outcomes which could potentially lead to systematic selection of socially desirable responses.

KAB comparison among medical schools

We found significant differences in all components measured among students in the three medical schools before the module was implemented. This could be related to differences in local condition such as curriculum structure and student years of education.

In UMCU, the Clinical Epidemiology (CE) and the EBM are taught in separate modules; the CE is taught in the 3rd year while the EBM in the 6th

year. In UI, the CE-EBM module is given in blocks as a four weeks module, but the students had also already learned about research methodology and biostatistics which was taught during their 1st year. In UM the CE-EBM is taught twice a week within the Social Preventive Medicine module which was conducted over three months. The fact that the UMCU students achieved the highest baseline score in all components compared to UI and UM shows that their previous CE module might have significantly contributed to their knowledge, attitude and behavior toward EBP.

The UI students scored higher than the UM students in knowledge, attitudes and future use of EBM which could also be related to previous exposure during research module in UI and the difference in students education years (4th year in UI vs 3rd year in UM). All the behavior questions asked about how frequent the students accessed different kinds of medical evidence such as text books, Medline and Cochrane database. Even though access to medical literature in UM is generally better than UI, similar behavior was found among the students in the two medical schools.

Similar conditions were still observed in the three medical schools after the module was implemented; the knowledge and attitude score of the UMCU students are still higher compared to the two Asian schools. Even though significant changes in EBP knowledge of UMCU and UM students were found after the module, the actual effect size were small. CE and EBM modules in UMCU have been implemented for 7 years after revision of the curriculum; even with higher pre-module scores, EBM teaching still adds knowledge to the UMCU students, however small.

Cultural differences in responding to the 6-point Likert scale format of the questionnaire which required the students to choose between strongly disagree to strongly agree could also influence the result. Further analysis of each scale selection revealed that the UI and UM students were more

likely to select the middle point (agree or disagree) when expressing their opinions compared to their Dutch colleagues who were more bold and did not hesitate to express stronger opinions. This is similar to other studies that compared American students with Asian students (Chinese and Japanese). (9, 10) The Asian students were more likely than the Americans to use the midpoint on the scales. However, students' uncertainty about their answer could also contribute to the selection of the midpoint.

The similarity between the scores achieved by the UI and UM students with what has been observed by Johnston et al in Hong Kong medical school (7) confirms our view. Moreover only an increase in EBP knowledge was observed in both studies. Nevertheless a more recent study also by Johnston (11) reported that attitudes and behavior could also increase after the module and Cheng et al (12) in National Taiwan University Taipei found improvement in all components after the module. Post module assessment in our study was conducted on the last day of the module which was run as a stand-alone module (in UI and UMCU) or integrated with Social and Preventive Medicine module (in UM) as opposed to being incorporated with the clinical rotation as in the studies by Johnston (11)and Cheng(12). Because of that, it is not sufficient to observe changes in attitude as well as application or behavior. Further learning experience which enables the students to implement the knowledge and skills they learned during the module is needed if we want to use the questionnaire as evaluation tools for teaching and learning in EBP.

Future application of the KAB questionnaire - The questionnaire includes different aspects on knowledge, attitudes, behavior and future use of EBP principles as described in Sicily statement(1). These aspects are suggested as dimensions for evaluation of EBP learning in the CREATE framework. (13) Still, the questionnaire does not sufficiently reflect all the EBP principles of asking, searching, appraising, integrating and evaluating separately.

Our data shows that this KAB questionnaire is helpful in providing information on the differences in knowledge, attitude, behavior and future use of EBP in three different medical schools in Asia and Europe prior to EBP teaching. Moreover it has been shown to pick up changes in the knowledge of students, even with higher pre-module scores. This KAB questionnaire can perhaps be used as an instrument to facilitate reflection of KAB for EBP. However, cultural aspects might influence the response and the changes in the attitude and behavior could not be observed immediately at the end of the EBP teaching (so no direct effects on these two dimensions). Further teaching program which enable the students to implement the knowledge and skills they learned during the module is needed if we want to use the questionnaire as evaluation tools for teaching and learning in EBP.

Conclusion

We show that EBP teaching has direct short term effects on knowledge but not on attitude. The validated KAB questionnaire is very useful and helpful in evaluating the effects of EBP teaching. It has managed to provide information on the pre-EBP module differences in knowledge, attitude, behavior and future use of EBP in three different medical schools in Asia and Europe, and on the post-EBP module change in knowledge.

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Chapter 8 General Discussion

Is Evidence-based Practice relevant to Indonesia?

With a population of approximately two hundred and fifty million, Indonesia is the fourth most populated country in the world. As a low-middle income country, Indonesia is currently facing significant health challenges. One of the challenges is the double burden of diseases which is caused by rapid epidemiologic transition. Currently, Indonesia still struggles to control infectious diseases such as tuberculosis, dengue hemorrhagic fever and malaria. Tuberculosis prevalence is 647 per 100,000 inhabitants, with mortality rate of 41 per 100,000 inhabitants per year[1] which positions Indonesia among the 22 countries with a "high burden" of tuberculosis. On the other hand, the prevalence of non-communicable diseases such as cardiovascular diseases and diabetes is also rising. In 2012, 36% of the total years of life lost (YLL) in Indonesia was due to communicable diseases while 55% was due to non-communicable diseases.[1] Cardiovascular disease has become the number one cause of death in the country since 1992[2], while prevalence of diabetes increased from 5.7% in 2007 to 6.9% in 2013(3) and an increase by 80% is foreseen between 2013 and 2035.[4, 5]

The epidemiologic transition is driven by a multitude of factors which include social and economic growth, urbanization, and globalization of technologies and food production.[6] Indonesia is the largest economy in Southeast Asia and is one of the emerging market economies of the world. Following the country's rapid development in the 1970s, the urbanization which has been driven by the rural-urban migration has increased tremendously. In 1950, 15% of Indonesia's population lived in urban areas. Forty years later, in 1990, this number doubled to 30%, and in 2015, 53% of the Indonesia's population lived in urban areas.[7]

Urbanization usually leads to changes in the life-style such as adoption of a more sedentary life-style and change in the dietary habits, both of which are the key risk factors for non-communicable diseases, in particular

diabetes. Although the types of carbohydrate sources in Indonesian diet are traditionally various, currently due to the national development policy in the previous era, almost half of the Indonesian general population diet consists of white polished rice.[8] As a result, glycemic load is high and the typical individual in Indonesia consumes more than double the carbohydrates necessary for body function, while the fiber intake is low (less than half of what is needed).[9] Low fiber intake leads to abdominal obesity, which is strongly associated with increased risk of diabetes.[10]

The effort to manage the non-communicable disease problems in Indonesia is being complicated by the inadequacy of the health human resources and facilities. The density of health workers and health facilities are low, as there are currently on average 20 doctors for every 100,000 inhabitants,[11] which is well below the South East Asia Region (SEARO) average of 58 and the world average of 142 per 100,000 inhabitants.[1] Moreover, health workers and health facilities have a skewed distribution (ranging from 9-68 doctors) while the population density among Indonesia's 35 provinces shows large variation (range from 5 to 17,000 population per kilometer square). With over 17,000 islands, Indonesia is the world's largest archipelagic country. Adequate distribution of health workers and facilities to the 900 of these islands which are permanently inhabited is a challenging task. Since 2014, Indonesia has established universal health coverage and faced the challenge of serving its large population with rather resources limitation. While effective and efficient use of the health resources is crucial, a survey conducted among primary health centers in eight most developed provinces revealed that few have proper equipment available, including equipment for diagnosing complications among the diabetic population.[12] While the latest calculation of the International Diabetes Federation predicts that there are approximately 10 million adults with diabetes in Indonesia[13], the complexity of the health problems of the Indonesian diabetic population has increased due to the low proportions of patients achieved blood glucose control.

Evidence-based Practice (EBP) is about improving the safety and effectiveness of health care through the integration of clinical expertise with the best available evidence. This is especially important in situations with major and severe health problems where it is vital that scarce resources are not wasted.[14] Although EBP is a concept which originated from developed countries, its implementation in developing countries like Indonesia is highly relevant.

From Evidence-based Practice to knowledge translation

The concept of Evidence-based Practice (EBP) has been actively disseminated in Indonesia since the year 2000 by a small group of pediatricians who conducted several workshops at medical schools and academic hospitals all over the countries.[15] In 2007, the development of Evidence-based Practice in Indonesia was fueled through the establishment of Asialink Clinical Epidemiology (CE) and Evidence-based Medicine (EBM) Project. The project, which involved two European universities (Utrecht and Oxford) and two Asian universities (University of Malaya and Universitas Indonesia), has managed to complete a range of activities in three years which include postgraduate courses on Clinical Epidemiology and Evidence-based Medicine, Master and PhD program, development of an Evidence-based Medicine curriculum for undergraduates, and establishment of a CE-EBM unit at the Faculty of Medicine Universitas Indonesia (FMUI) - Cipto Mangunkusumo Hospital (CMH), Jakarta in 2010.[15, 16]

While the content and the materials of the Clinical Epidemiology and Evidence-based Medicine courses were originally developed by the staffs of the University Medical Center Utrecht and Oxford University and the lectures were initially conducted by them, the courses were gradually being handed over to the local teachers whose knowledge and skills were enhanced through participation in teaching workshops or a PhD program in Oxford

or Utrecht. Until now, even though the project has finished, the courses are still being conducted regularly in Jakarta by the newly established CE-EBM center.

In Indonesia, the 2006 and 2012 version of the Standard of Medical Doctors' Competencies developed by Indonesian Medical Council has recognized Evidence-based Practice as one of competencies which should be achieved by the medical graduates.[17, 18] However, there is also a wide variation on the degree of the integration of the Evidence-based Practice in the Indonesian medical curriculum. A process to adapt a Clinical Epidemiology and Evidence-based Medicine module which is originated and already implemented in the University Medical Center Utrecht to fit to the local context of two medical schools in Jakarta and Kuala Lumpur is described in this thesis. The module is successfully implemented in both schools and comparable improvement on knowledge was seen in Utrecht, Jakarta and Kuala Lumpur, although due to the short follow-up, changes in attitude and behavior remain to be seen and it may take decades to achieve sufficient number of health care practitioners that have competencies in Evidence-based Practice.

The CE-EBM unit of the Faculty of Medicine Universitas Indonesia – Cipto Mangunkusumo Hospital and the already established Clinical Epidemiology and Biostatistics Unit (CEBU) of Gadjah Mada University at Yogyakarta then formed the Indonesian Clinical Epidemiology and Evidence-based Medicine (ICE-EBM) network in 2011 which now has 15 institutions all over Indonesia as its members. The main objective of the network is to promote CE and EBM by organizing and conducting CE and EBM capacity building activities in Indonesia. One of the current efforts to improve Evidence-based Practice is through translation of Cochrane systematic reviews summary in-collaboration with the Australasian Cochrane Center.

Although the development of the knowledge and skills on Evidence-based Practice in Indonesia seems promising, it is still not enough to achieve improvement in health care. To achieve health benefits, the evidence must be moved into action. The efforts that are aimed at integrating Evidence-based Practice in to daily clinical practice is now an increasing issue and known as "knowledge translation".[19, 20]

Knowledge translation on diabetes in Indonesia

One of the key obstacle in the progress of health systems in many low- and middle-income countries (LMICs) is the failure to effectively implement evidence-informed interventions. This results in the failure to achieve the United Nations' Millennium Development Goals (MDG). Several features unique to the low-and middle-income countries add another layer of complexity in the implementation of evidence, particularly a high burden of disease which is compounded by extreme shortages of human and material resources. Since both of these factors complicate the uptake and implementation of evidence from research into policy and practice, efficient knowledge translation is required.[21, 22]

A conceptual framework by Graham et al breaks the knowledge translation process in to knowledge creation and knowledge application (action cycle). Knowledge creation, or the production of knowledge, is composed by three phases: knowledge inquiry, knowledge synthesis, and creation of knowledge tools. As knowledge is distilled through each stage in the knowledge creation process, the resulting knowledge becomes more synthesized and potentially more useful to the end-users.[19, 23]

Knowledge inquiry includes the completion of primary research. A systematic review by Bazargani et al. in 2014 reported "research barriers" as the most dominant barrier to Evidence-based Practice implementation.

Research barriers include, among others, methodological problems, poor generalizability and limited relevance of research to practice.[24] As published research mostly comes from high-resources countries, the relevance and applicability of its findings for low-resources settings is a continuously returning question.[25] However, there is only limited knowledge inquiry going on in the lower-and middle-income countries like Indonesia. Indonesia is the third most populous developing country after China and India, yet the number of published research from Indonesia is far behind the two countries [26]. Moreover, we found that only a small proportion of the published research from Indonesia has sufficiently high quality of reporting and methods. Particularly on diabetes care, a literature review conducted by Soewondo et al in 2013 identified very few publications to accurately estimate the burden, expenditure, treatments, complications and outcomes of treatment for diabetes in Indonesia.[27] Therefore, although there is clearly a need in Indonesia to follow the conceptual framework of knowledge translation, so far little efforts in research, practice and policy have been made to do so.

The synthesis stage brings together the disparate research findings that may exist globally on health and health care topics and attempts to identify common patterns. Systematic reviews are the foundation of most activities related to knowledge translation.[20] Chinnock et al. called for more systematic reviews which include health problems that are priorities, as well as interventions that are affordable and feasible in the developing countries.[25] However, in our assessment on the quality of reporting of the risk of bias of the Indonesian medical research, we found only three systematic reviews which involve Indonesian researchers that were published in 2008-2010; one of it is on diabetes treatment.

At the stage of development of tools and products, the best-quality knowledge is further synthesized and distilled into decision-making tools such as practice guidelines, aids for patient decisions or algorithms.

For low-resources countries, adaptation of guidelines is either conducted as an alternative to de novo guideline development or to improve guideline implementation through local tailoring of an international guideline.[28] Adaptation is also identified as an important step toward reducing duplication in the development of guidelines, which can result in a tremendous cost in financial and human resources.[29] However, during the adaptation process, implementation of Evidence-based Practice principles still need to be adhered to[30] as evidence-based recommendations were used more than recommendations for practice that were not based on research evidence.[31] Using the Appraisal of Guidelines, Research and Evaluation Collaboration (AGREE II) instrument[32], we assessed the methodological quality of an Indonesian diabetes guideline and we found that it was lower than the international diabetes guidelines that were used as sources for being adapted (i.e. parent guidelines).

The second part of the knowledge translation process is knowledge application or the "action cycle". The cycle involves identifying the problem; identifying, reviewing and selecting the knowledge to implement; adapting or customizing the knowledge to the local context; assessing the determinants/barriers of knowledge use; selecting, tailoring, implementing and monitoring interventions related to knowledge translation; evaluating outcomes or impacts of using the knowledge; and determining strategies for ensuring sustained use of knowledge.[19]

One important health issue in diabetes care in Indonesia is that more than 60% of patients do not achieve blood glucose control.[27] While clinical practice guidelines are believed to be one of the strategies to improve the quality of care, our study found that the adherence to the recommendations on the Indonesian type 2 diabetes guidelines is very low.[33] Identifying the gaps from knowledge to practice is the starting point of implementing knowledge. Using the awareness to adherence model by Pathman et al, we learned that there are four stages in the "evidence to action" pathway, namely awareness, agreement, adoption, and adherence. When selecting

the appropriate intervention to promote the incorporation of best evidence into the practices of health professionals, we should consider the different determinants at each step of this pathway.[34, 35]

What could be improved?

Knowledge translation is yet to be introduced in Indonesia and the current policy of the Indonesian government is still focusing on the improvement of knowledge creation. Currently, many incentives have been provided by the Indonesian government for Indonesian scientists who published in international journals. The health professions working on diabetes field should focus more on publishing good quality patient-oriented research concerning diagnosis, prognosis, and therapy in which patient-oriented outcomes are evaluated. Yet we are not only in need of higher investments in producing biomedical research, but also in the dissemination and organization of research findings, and in adapting source information into end-user products that are easily accessible, readable, reliable, and relevant.[36] As higher proportion of health professionals in Indonesia are less familiar with the dominant scientific language of English[26] effort to translate the best available and relevant evidence such as Cochrane systematic reviews should be prioritized.

Implementation of evidence-based clinical practice guidelines is one way to make evidence-based care visible. Therefore, more reliable evidence-based clinical practice guidelines that fit the local context should be produced by the professional organizations in collaboration with government, especially for common conditions associated with a high disease burden.[37] While the adaptation of existing high-quality guidelines will still be preferred as the most efficient strategy, the results should be presented in user-friendly, implementable formats.

Capacity building activities in EBP should be continuously performed, whether in collaboration with internationally renowned institutions or through nation-wide

networking like the Indonesian Clinical Epidemiology and Evidence-based Medicine (ICE-EBM) Network. We proposed a roadmap on the Evidence-based Practice and knowledge translation on diabetes care in Indonesia (table 1). The emphasis of the capacity building should not only on teaching the science of Evidence-based Practice but also on its practical application to patient care and targeting the competence on knowledge translation.[38]

The success in the integration of Evidence-based Practice in the medical school curricula should be followed by improvements in the curriculum to incorporate sessions on methods for incorporating Evidence-based Practice in the daily routine, so the medical graduates will be more ready to apply it when they practice.

Conclusion

Although the capacity building activities on Evidence-based Practice among the health profession in Indonesia are growing, some gaps in the knowledge production and application especially on diabetes care were identified. The gaps on the knowledge production include limited number and low quality of evidence on diabetes care, very little production of systematic reviews on the problems related to diabetes care which are relevant to Indonesian situation and low rigor of development as well as low applicability of the existing diabetes guidelines. Using the "awareness to adherence" model we found that following awareness, there were decreasing rates on the agreement, adoption and finally adherence. The remaining gaps should be assessed thoroughly using rigorous methods and involving relevant stakeholders. The effort should be followed by the continuous action cycle of the knowledge translation process. Promoting the knowledge translation process should be done simultaneously with the Evidence-based Practice capacity building to achieve improvement in health care in a developing country like Indonesia.

Table 1. Roadmap on the Evidence-based Practice and knowledge translation on diabetes care in Indonesia

		Current situation in Indonesia (as identified in this thesis)	**Proposed action**	**Leading sector**
Evidence-based Practice		Undergraduates and post-graduates capacity building activities are increasing, supported by national and international network.	Improvement of the Evidence-based Practice teaching activities to incorporate knowledge translation competency	Academic community
Knowledge translation				
Knowledge creation	Knowledge inquiry	Limited number of published evidence on diabetes care; low quality of the evidence	More publication of patient-oriented diabetes research concerning diagnosis, prognosis, and therapy in which patient-oriented outcomes are evaluated	Academic community supported by the ministry of research and higher education
	Knowledge synthesis	Very few systematic review published on the health problems that are relevant to the Indonesian diabetes care	More production of relevant systematic review on diabetes care and translation of available Cochrane Systematic Reviews	Academic community
	Creation of knowledge tools	One adapted guidelines on diabetes with low rigour of development and low applicability	Engage multiple stakeholders including experts in guideline development. Apply an evidence-based methods in guidelines adaptation such as the ADAPTE method. Provide supporting tools for implementation.	Professional organization in collaboration with the ministry of health
Knowledge application	Identifying gaps	Low adherence to diabetes guidelines recommendations despite high awareness. From awareness, there were decrease on the agreement, adoption and adherence to diabetes guidelines.	Complete assessment of the gaps using rigorous methods which includes perspectives from other relevant stakeholders.	Professional organization in collaboration with the ministry of health and the health care providers
	The finding on the gaps should be followed by the next action: ● Identifying, reviewing and selecting knowledge to implement ● Adapting or customizing the knowledge to the local context ● Assessing the determinants/ barriers of knowledge use ● Selecting, tailoring, implementing and monitoring interventions ● Evaluating outcomes or impacts ● Determining strategies for ensuring sustained use of knowledge			All of the above

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Summary

In **chapter 1,** a general introduction, the aim and outline of this thesis are presented. In this chapter, we describe the burden of diabetes in Indonesia and the current effort to provide an evidence-based diabetes care in Indonesia.
In **chapter 2,** we explored the variation in diabetes prevalence across Asian countries and determine to what extent the variation may be explained by differences in the health system components and the existence of known risk factors of non-communicable diseases (NCDs) such as sedentary life-style, hypertension and obesity. We conducted an ecological analysis which utilizes publicly available data from the World Health Organization (WHO), World Bank (WB), and International Diabetes Federation (IDF). Variation in diabetes prevalence across Asian countries was examined using control charts. We found that there is considerable geographical variation in diabetes prevalence across 36 Asian countries. Special-cause variation (variation that is not expected of a stable process) in diabetes prevalence is found in 58% of the Asian countries; nine countries were below the 99.8 percent control limits while twelve were above it. Fifteen (42%) Asian countries suggest common-cause variation (variation that is expected of a stable process). Although a substantial part of this variation could be explained by the differences in quality of health care governance, hypertension prevalence and obesity prevalence. Further study is needed to identify special practice or process related to diabetes that are particular to these regions in Asia, in order to promote effective public health intervention in the prevention of diabetes.

In **chapter 3,** we present the results of a survey to assess the degree of awareness, agreement, adoption and adherence of general practitioners (GPs) in Indonesia to type 2 diabetes mellitus guidelines, and their association with characteristics of the responders. We found that of the 399 GPs participating, 89% was aware of the existence of Indonesian type 2 diabetes guidelines. Awareness for each of the seven recommendations varied from 66% to 91%. The recommendation to use a random blood

glucose test for diagnosing patients with classic diabetes symptoms had the least awareness (66%) and least agreement (41%). The recommendation on statin use was the least adopted (48%), while the least adherence (2%) was found for the recommendation on screening for diabetes for patients with risk factors. Years of practice experience and proportion of diabetes patients seen in their practice were independently related with the adherence to statin prescription. We conclude that high awareness of the Indonesian type 2 diabetes guideline does not necessary lead to adoption or adherence to guidelines. The awareness-to-adherence model helps in identifying barriers for the use of guidelines.

Most of the clinical guidelines in low-resource countries are adaptations from pre-existing international guidelines. These adaptation can be problematic when those international guidelines are not based on current evidence or original evidence-based international guidelines are not followed. In **chapter 4**, we evaluate the quality of an Indonesian type 2 diabetes guideline (Perkeni's guideline 2011) adapted from four international guidelines. The parent guidelines were from the International Diabetes Federation (IDF) 2005, the American Association of Clinical Endocrinologist (AACE) 2007, the American Diabetes Association (ADA) 2010 and one which was jointly released by ADA and European Association for the Study of Diabetes (EASD) 2009. We found that the Perkeni's guideline satisfied 55% of the Appraisal of Guidelines, Research and Evaluation Collaboration (AGREE II) items, while its parent guidelines satisfied 59% to 74%. Perkeni's shows low score on "rigor of development" and "applicability" and the lowest score in the "scope and purpose" domain. Differences were found in four recommendations: the screening of diabetes, control of hyperglycemia, target blood glucose and treatment of dyslipidemia. In three out of those four, Perkeni followed the ADA's recommendation. Based on that, we concluded that the process underlying the Indonesian type 2 diabetes

guideline development is curtailed due to being under-resourced and the use of the cited suboptimal source guidelines might risk the validity of the recommendations it contains. Implementation of Evidence-based Practice principles such as those proposed by ADAPTE collaboration should be adhered to when guideline are derived from other guidelines to be used in other than its original context or circumstances.

Since published clinical evidence is one component of Evidence-based Practice, we conducted an evaluation of the quality of reporting of the risk of bias of the Indonesian medical research. In **chapter 5,** we assess publications from PubMed and non-PubMed indexed Indonesian medical journals for risk of bias based on a combination of the Hedges-criteria and the Oxford Center for Evidence-based Medicine criteria. We assessed whether the publications addressed the risk of bias adequately (quality of reporting) and whether the risk of bias criterion was fulfilled (quality of methods). Of the 1753 publications, 29% was original medical research. For 21% the quality of reporting was high; for 15% the quality of methods was high. The proportion of high quality was significantly higher among PubMed than non-PubMed indexed studies, with 12% (95% CI of difference 3;23) difference between proportions. As we found only a small proportion of Indonesian studies which have high quality reporting or methods, we recommend to endorse and follow international reporting guidelines to improve the quality of future studies.

Clinical Epidemiology (CE) and Evidence-based Medicine (EBM) have become important parts of medical school curricula all over the world. In **chapter 6**, we report the process of adaptation and implementation of an integrated CE and EBM module in the Faculty of Medicine Universitas Indonesia (UI), Jakarta and in the University of Malaya (UM) in Kuala Lumpur. The module was originated from and already implemented in the University Medical Center Utrecht (UMCU). Before the start of the

module, UI and UM staff followed a training of teachers (TOT). The TOT was well received by staff in Jakarta and Kuala Lumpur, and after adaptation the CE and EBM modules were integrated in both medical schools. The pre-test results of UI and UM were significantly lower than those of UMCU students ($p<0.001$). The post-test results of UMCU students were comparable ($p=0.48$) with UI, but significantly different ($p<0.001$) from UM. Common problems for the modules in both UI and UM were limited access to literature and variability of the tutors' skills. We learned that adoption and integration of an existing Western CE-EBM teaching module into Asian medical curricula is feasible while learning outcomes obtained are quite similar.

Direct short term effects of a Clinical Epidemiology and Evidence-based Medicine (CE-EBM) module on the knowledge, attitude and behavior of students in the University Medical Center Utrecht (UMCU), Universitas Indonesia (UI) and University of Malaya (UM) were reported in **chapter 7**. For the assessment, we used an adapted version of a 26-item validated questionnaire, including 4 subscales: knowledge, attitude, behavior, and future use of Evidence-based Practice (EBP). In total, 526 students (224 UI, 202 UM and 100 UMCU) completed the questionnaires. We found that in the 3 medical schools Cronbach's alpha for the pre-module total score and the 4 subscales scores always exceeded 0.6. UMCU students achieved the highest pre-module scores in all subscales compared to UI and UM. The CE-EBM module significantly ($p<0.001$) increased the knowledge of the UMCU and the UM students but not or the UI. The post-module scores for attitude did not change in the three medical schools. Based on that we realized that EBP teaching had direct short term effects on knowledge, not in attitude. Differences in pre-module scores are most likely related to differences in the system and the infrastructure of both medical schools and their curriculum.

In **chapter 8,** we argue that Evidence-based Practice (EBP) is especially important in situations with major and severe health problems where it is vital that scarce resources are not wasted. Although EBP is a concept which originated from developed countries, its implementation in developing countries like Indonesia is highly relevant. However, although the development of the knowledge and skills on EBP in Indonesia seems promising, to achieve health benefits, the evidence must be moved into action. The efforts that are aimed at integrating Evidence-based Practice in to daily clinical practice (the "knowledge translation effort) is now an increasing issue. Throughout the chapters some gaps in the knowledge production and application especially on diabetes care were identified. The gaps on the knowledge production include limited number and low quality of evidence on diabetes care, very little production of systematic reviews on the problems related to diabetes care which are relevant to Indonesian situation and low rigor of development as well as low applicability of the existing diabetes guidelines. Using the "awareness to adherence" model we found that following awareness, there were decreasing rates on the agreement, adoption and finally adherence. The remaining gaps should be assessed thoroughly using rigorous methods and involving relevant stakeholders. The effort should be followed by the continuous action cycle of the knowledge translation process. In the end, we conclude that promoting the knowledge translation process should be done simultaneously with the Evidence-based Practice capacity building to achieve improvement in health care in a developing country like Indonesia.

Samenvatting

In **hoofdstuk 1** worden het doel en de opzet van dit proefschrift uitgelegd. Eerst wordt de prevalentie van diabetes in Indonesië beschreven, waarna de huidige inspanningen in Indonesië om evidence-based diabeteszorg in te voeren worden toegelicht.

In **hoofdstuk 2** wordt aandacht besteed aan de variatie van de prevalentie in diabetes in de diverse Aziatische landen en de mate waarin deze variatie kan worden verklaard door verschillen in de opzet van de gezondheidszorg en de bekende risicofactoren voor niet-infectieuze ziekten zoals lifestyle, hoge bloeddruk en overgewicht. Wij voerden een ecologische analyse uit op basis van de beschikbare gegevens van de Wereldgezondheidsorganisatie (WHO), de Wereldbank (WB) en de Internationale Diabetes Federatie (IDF). Bij de analyse van de variatie in de prevalentie van diabetes in 36 Aziatische landen bleek dat er sprake is van een aanzienlijke geografische variatie in deze prevalentie. In 15 (42%) van de Aziatische landen kon de variatie verklaard worden op basis van 'common-causes' (variatie binnen een stabiel proces). Een aanzienlijk gedeelte van deze variatie kan worden verklaard uit verschillen in kwaliteit van gezondheidszorg, bestuur en de prevalentie van hypertensie en obesitas. Voorts bleek dat in 21 (58%) van de Aziatische landen de variatie in de prevalentie van diabetes verklaard kon worden door de zogenaamde 'special-cause' variatie (de variatie die men niet verwacht in een stabiel proces), waarbij negen landen onder de 99.8% controle limiet scoorden en twaalf daarboven. Hierbij moet gedacht worden aan speciale praktijk- of proces gerelateerde factoren in diabeteszorg. In deze Aziatische gebieden is nader onderzoek nodig naar deze factoren, zodat effectieve public health interventies ter preventie van diabetes kunnen worden ingezet.

In **hoofdstuk 3** presenteren wij het resultaat van een enquête die gebaseerd is op het zogenaamde 'awareness-to-adherence' model, waarbij 'de

bekendheid met','het eens zijn met', 'het overnemen van' en het 'houden aan' de richtlijnen met betrekking tot diabetes door Indonesische huisartsen voor diabetes type 2 werd uitgevraagd. Ruim 89% van de respondenten was zich bewust van het bestaan van de Indonesische richtlijnen over type 2 diabetes. Bekendheid met alle aanbevelingen in de richtlijnen varieerde afhankelijk van de achtergrond en kenmerken van de respondent van 66% tot 91%. De aanbeveling om een willekeurige bloedglucose te gebruiken om patiënten met de klassieke diabetes symptomen op te sporen, was het minst bekend (66%) en 41% was het er niet mee eens. De aanbeveling om statines voor te schrijven was het minst geaccepteerd (48%) en aan de aanbeveling om te screenen op diabetes voor patiënten met risicofactoren kon rekenen op de minste bijval en uitvoering (2%). Het voorschrijven van een statine hing samen met enerzijds het aantal jaren praktijkervaring en anderzijds de hoeveelheid patiënten met diabetes in de praktijk. Wij concluderen dat grote bekendheid met de Indonesische richtlijn niet noodzakelijkerwijs resulteert in het volgen van die richtlijn of het implementeren van toepassing daarvan in de dagelijkse praktijk.

In landen met beperkte middelen, zijn de meeste klinische richtlijnen overgenomen uit al langer bestaande internationale richtlijnen. Deze overname en aanpassing kan problemen opleveren wanneer de internationale richtlijnen niet gebaseerd zijn op het laatste wetenschappelijk bewijs of indien de originele evidence-based internationale richtlijnen niet worden gevolgd.

In **hoofdstuk 4** evalueren we de kwaliteit van de Indonesische richtlijn voor diabetes type 2 patiënten (Perkeni guideline 2011) die is afgeleid van 4 internationale richtlijnen: de International Diabetes Federation (IDF), de American Association for Clinical Endocrinologist (AACE), de American Diabetes Association (ADA) en een gezamenlijke richtlijn van ADA en de European Association for the Study of Diabetes (EASD). Wij stelden vast dat de Perkeni richtlijn voldoet aan 55% van de AGREE II criteria (Appraisal of Guidelines, Research and Evaluation Collaboration), terwijl dit

voor de oorspronkelijke richtlijnen varieert van 59% tot 74%. De Perkeni richtlijn had een lage score voor de onderdelen 'strikte ontwikkeling' en 'toepasbaarheid' en de laagste score binnen het domein 'uitgebreidheid' en 'doelstelling'. Er werden verschillen vastgesteld voor 4 aanbevelingen: de screening op diabetes, controle van hoge bloedsuikers, de streefwaarde van de bloedsuiker en behandeling van dyslipidemie. Bij 3 van de 4 aanbevelingen volgde Perkeni de ADA aanbeveling. Wij stellen dan ook vast dat de wijze waarop de aanbevelingen zijn afgeleid van de oorspronkelijke richtlijnen en worden toegepast in de context van de Indonesische gezondheidszorg de noodzakelijke transparantie mist. Vandaar dat evidence-based- practice principes moeten worden gevolgd en uitgevoerd wanneer richtlijnen alleen of tegelijkertijd worden afgeleid van andere richtlijnen of worden aangepast in een andere context.

Een belangrijke component van de evidence-based-practice is het feit dat het klinisch bewijs is gepubliceerd. Wij onderzochten of de kwaliteit van de publicaties en de kans op bias van medisch onderzoek afkomstig uit Indonesië (**hoofdstuk 5**) afhankelijk is van indexering van het betreffende tijdschrift in Pubmed. Voor de beoordeling van de kwaliteit en de kans op bias gebruikten wij de Hedges-criteria en de criteria van het Oxford Center for Evidence Based Medicine. Van de 1753 publicaties, betrof 29% oorspronkelijk medisch onderzoek. Van 21% van deze publicaties was de kwaliteit van de rapportage voldoende en van 15% was de kwaliteit van de methoden voldoende. Met een verschil van 12% (95% betrouwbaarheidsinterval van het verschil 3%; 23%), was de kwaliteit van de in PubMed geïndexeerde studies duidelijk beter. Het aantal goed opgezette studies uit Indonesië is beperkt, en de kwaliteit van de methoden en de kwaliteit van de rapportage van het Indonesisch onderzoek kan aanzienlijk verbeterd worden.

In **hoofdstuk 6** doen wij verslag van de introductie van de cursus geïntegreerde Klinische Epidemiologie (KE) en Evidence-based Medicine (EBM) in het

curriculum van de medische faculteit van 'Universitas Indonesia' in Jakarta en de Úniversity of Malaya' in Kuala Lumpur, Maleisië. Deze cursus werd voor de studenten van de medische faculteit in Utrecht ontworpen. Voor de invoering van de cursus volgden de Indonesische en Maleisische staf de 'train de trainer' cursussen. Voordat de studenten met de cursus begonnen en na afloop daarvan werden testen afgenomen om het niveau van inhoudelijke kennis te bepalen. De kennis en ervaring van de Indonesische studenten (n= 196) en Maleise studenten (n=160) voorafgaande aan de cursus bleek significant minder in vergelijking tot de studenten (n=389) van de Medische faculteit Utrecht ($p<0.001$). De resultaten van de Utrechtse studenten na afloop van de cursus waren vergelijkbaar ($p=0.48$) met de Indonesische studenten maar verschilden belangrijk met die van de Maleisische studenten. Veel voorkomende problemen met de modules in zowel Indonesië als Maleisië waren de beperkte toegang tot literatuur en variatie in de kwaliteiten van de docenten. Wij stelden vast dat het overnemen en integreren van een bestaand Westerse onderwijs module voor KE en EBM mogelijk is terwijl de uiteindelijke resultaten in termen van toename van inhoudelijke kennis vergelijkbaar en bevredigend zijn.

In **hoofdstuk 7** worden de korte termijn effecten van de bovengenoemde cursus op de kennis, attitude en het gedrag van de studenten in Utrecht, Indonesië en Maleisië gerapporteerd. Er werd een aangepaste versie van een 26-item gevalideerde vragenlijst gebruikt met 4 subklassen: kennis, attitude, gedrag en toekomstig gebruik van EBM. In totaal 526 studenten vulden de vragenlijsten in (224 in Indonesië, 202 in Maleisië en 100 in Utrecht). Voor de cursus was de Cronbach's alfa voor de totale score en de 4 subklassen altijd hoger dan 0.6 voor alle 3 medische faculteiten. De Utrechtse studenten hadden voor aanvang van de cursus de hoogste score in alle subklassen vergeleken met de Maleise en Indonesische studenten. Na afloop van de cursus bleek dat de toename van kennis voor de Utrechtse en de Maleise studenten statistisch significant ($p<0.001$) was maar voor de

Indonesische studenten niet. Na afloop van de cursus bleek de attitude voor alle 3 de medische faculteiten niet veranderd te zijn. Onderwijs op het gebied van Klinische Epidemiologie en EBM had een direct korte termijn effect op kennis maar niet op attitude. De verschillen tussen de groepen voorafgaand aan de cursus hangt hoogst waarschijnlijk samen met het onderwijssysteem, infrastructuur en inrichting van het curriculum.

In **hoofdstuk 8** bepleiten wij de stelling dat evidence-based-practice belangrijk is in situaties waarbij sprake is van grote en ernstige gezondheidszorg problemen omdat het van groot belang is dat beperkte middelen niet worden verspild. Ofschoon evidence-based practice een concept is dat oorspronkelijk uit ontwikkelde landen komt, is de implementatie ervan in ontwikkelingslanden zoals Indonesië zeer relevant. In toenemende mate wordt In Indonesië aandacht besteed en daadwerkelijke geprobeerd evidence-based-practice in de dagelijkse klinische praktijk te integreren. Ofschoon de ontwikkeling van de kennis en vaardigheden op het gebied van evidence-based practice in Indonesië veelbelovend geacht worden, moet er nog wel het een en ander op dit terrein gebeuren voordat de vruchten ervan kunnen worden geplukt.

In de verschillende hoofdstukken stelden wij diverse tekortkomingen vast met betrekking tot het genereren en toepassen van kennis op het gebied van diabeteszorg. Deze tekortkomingen zijn: de beperkte beschikbaarheid van wetenschappelijk bewijs op het gebied van diabeteszorg dat meestal ook nog van een lage kwaliteit is. Daarnaast ontbreekt het in het beperkt aantal systematische reviews op het gebied van diabeteszorg aan informatie over de problemen die relevant zijn voor de Indonesische situatie. Voorts blijft ontwikkeling en de toepasbaarheid van de bestaande diabetesrichtlijnen achter bij de stand van de wetenschap en de praktijk van ontwikkeling van richtlijnen. Door het ‘awareness to adherence’ model toe te passen konden wij vaststellen dat ‘verbeterde bewustwording’ van een richtlijn gevolgd

wordt door ’het eens zijn met’, ‘het overnemen van’ en het ‘houden aan’ de richtlijn. De tekortkomingen in het gebruik en toepassing van richtlijnen, moeten worden aangepakt door bevordering van de betrokkenheid van alle relevante stakeholders en hanteren van strikte methoden van praktijkvoering. Daarbij is een continue cyclus van overdracht en toepassing van kennis en vaardigheden op gebied van Evidence Based Medicine van groot belang. Tot slot concluderen wij dat het bevorderen van kennisoverdracht moet samengaan met de opbouw en de ontwikkeling van kennis op het gebied van evidence-based practice om de gezondheidszorg in een land in ontwikkeling zoals Indonesië te bevorderen.

Ringkasan

Bab 1 menyajikan pengantar umum, tujuan dan *outline* disertasi ini. Pada bab ini, dijelaskan mengenai permasalahan diabetes di Indonesia dan upaya yang telah dilakukan dalam menyelenggarakan penatalaksanaan diabetes berbasis bukti.

Bab 2 menyajikan penelitian yang bertujuan menganalisis variasi prevalensi diabetes di negara-negara di Asia dan menentukan sejauh mana variasi tersebut dipengaruhi oleh perbedaan komponen pada sistem kesehatan dan terdapatnya faktor-faktor risiko penyakit tidak menular (PTM) seperti gaya hidup, hipertensi dan obesitas. Penelitian tersebut merupakan sebuah analisis ekologi yang menggunakan data-data yang telah dipublikasi oleh World Health Organization (WHO), World Bank (WB), dan International Diabetes Federation (IDF). Variasi prevalensi diabetes pada negara-negara Asia dianalisis dengan *control charts*. Terdapat variasi prevalensi diabetes secara geografis yang cukup besar pada 36 negara Asia. Ditemukan s*pecial-cause variation* (variasi yang tidak diduga ditemukan pada proses yang stabil) dalam prevalensi diabetes pada 58% negara-negara Asia. Sembilan negara berada di bawah garis 99,8 persen batas kontrol bawah sementara 12 negara berada di atas 99,8 persen batas kontrol atas. Lima belas (42%) negara Asia menunjukkan *common-cause variation* (variasi yang biasa ditemukan pada proses stabil). Sebagian variasi diketahui dipengaruhi oleh terdapatnya perbedaan pada kualitas kepemimpinan kesehatan (*health care governance*), prevalensi hipertensi dan prevalensi obesitas. Dalam rangka meningkatkan upaya kesehatan masyarakat dalam pencegahan diabetes, diperlukan penelitian lebih lanjut untuk mengidentifikasi praktik atau proses terkait diabetes yang secara khas ditemukan di berbagai wilayah di Asia.

Bab 3 menyajikan hasil survei yang menilai besarnya pengetahuan (*awareness*), persetujuan (*agreement*), adopsi (*adoption*) dan kepatuhan

(*adherence*) para dokter praktik umum (DPU) di Indonesia terhadap panduan penatalaksaan diabetes tipe 2, serta apakah keempat hal tersebut dipengaruhi oleh karakteristik responden. 89% dari 399 DPU Indonesia yang berpartisipasi pada survei ini mengetahui adanya panduan penatalaksanaan diabetes tipe 2 Indonesia. Pengetahuan terhadap ketujuh rekomendasi dalam panduan berkisar antara 66% hingga 91%. Tingkat pengetahuan terendah (66%) dan tingkat persetujuan terendah (41%) terdapat pada rekomendasi mengenai penggunaan pemeriksaan glukosa darah sewaktu dalam mendiagnosis diabetes pada pasien dengan gejala klasik diabetes. Rekomendasi mengenai penggunaan statin meraih tingkat adopsi terendah (48%) sementara rekomendasi mengenai skrining diabetes pada pasien dengan faktor risiko meraih tingkat kepatuhan terendah (2%). Lamanya praktik (dalam tahun) dan proporsi pasien diabetes yang ditemui di tempat praktik berhubungan secara independen dengan kepatuhan terhadap peresepan statin. Disimpulkan bahwa tingkat pengetahuan yang tinggi terhadap panduan penatalaksanaan diabetes tipe 2 Indonesia tidak selalu diikuti oleh adopsi maupun kepatuhan terhadap rekomendasi yang penting bagi penatalaksanaan dan hasil yang berkualitas. Model pengetahuan-kepatuhan (*awareness-to-adherence*) dapat membantu mengidentifikasi hambatan terhadap pemanfaatan panduan.

Sebagian besar panduan praktik klinis yang terdapat di negara-negara dengan sumber daya terbatas atau negara berkembang merupakan hasil adaptasi terhadap panduan internasional yang telah ada. Adaptasi dapat menimbulkan masalah saat panduan internasional yang diadaptasi bukan merupakan panduan yang berbasis bukti. Pada **bab 4,** dilakukan evaluasi terhadap kualitas panduan penatalaksanaan diabetes tipe 2 Indonesia (panduan Perkeni 2011) yang merupakan adaptasi empat panduan internasional. Panduan yang menjadi sumber adalah panduan yang diterbitkan oleh International Diabetes Federation (IDF) tahun 2005, American Association of Clinical Endocrinologist (AACE) tahun 2007, American Diabetes Association

(ADA) tahun 2010 dan satu panduan yang dikeluarkan bersama oleh ADA dan European Association for the Study of Diabetes (EASD) tahun 2009. Panduan Perkeni memenuhi 55% kriteria Appraisal of Guidelines, Research and Evaluation Collaboration (AGREE II), sedangkan panduan yang menjadi sumbernya memenuhi 59% hingga 74% kriteria. Panduan Perkeni memiliki skor rendah pada area "kecermatan penyusunan" dan "kemampu-terapan" (*applicability*), serta skor terendah pada area "lingkup dan tujuan". Ditemukan perbedaan pada empat rekomendasi yaitu skrining diabetes, pengendalian hiperglikemia, target glukosa darah dan penatalaksanaan dislipidemia. Rekomendasi Perkeni mengikuti ADA pada tiga dari empat rekomendasi tersebut. Disimpulkan bahwa proses penyusunan panduan diabetes tipe 2 Indonesia memiliki kelemahan yang disebabkan oleh keterbatasan sumber daya dan penggunaan panduan internasional yang tidak berkualitas terbaik sebagai sumber, sehingga berisiko menurunnya validitas rekomendasi yang dihasilkan. Prinsip *Evidence-based Practice* (EBP) seperti yang dianjurkan oleh ADAPTE *collaboration* harus diterapkan dan ditaati pada saat mengadaptasi satu panduan sebagai sumber panduan lain yang akan digunakan pada situasi yang berbeda.

Bukti klinik yang dipublikasi merupakan salah satu komponen *Evidence-based Practice* (EBP) yang penting. Oleh karena itu dilakukan suatu evaluasi terhadap kualitas pelaporan risiko bias pada penelitian kedokteran Indonesia. Pada **bab 5**, dilakukan telaah risiko bias terhadap publikasi Indonesia yang terindeks pada PubMed maupun yang terdapat pada jurnal kedokteran Indonesia yang tidak terindeks PubMed. Telaah risiko bias menggunakan kombinasi kriteria Hedges dan kriteria Oxford Center for Evidence-based Medicine. Dilakukan penilaian terhadap kualitas pelaporan (apakah publikasi telah melaporkan risiko bias secara memadai) dan kualitas metode penelitian (apakah publikasi memenuhi kriteria risiko bias). Dari 1753 publikasi yang ditemukan saat pencarian, 29% merupakan penelitian kedokteran primer. Kualitas pelaporan yang tinggi terdapat pada

21% publikasi sedangkan kualitas metode yang tinggi terdapat pada 15% publikasi. Proporsi penelitian dengan kualitas yang tinggi pada publikasi yang terindeks PubMed lebih besar secara bermakna dibanding pada yang tidak terindeks PubMed (perbedaan proporsi 12%, 95% CI 3;23). Dengan ditemukannya proporsi kualitas pelaporan maupun metodologi penelitian yang rendah pada publikasi Indonesia, kami menyarankan agar penggunaan panduan internasional pelaporan hasil penelitian dalam rangka peningkatan kualitas penelitian Indonesia di masa depan.

Epidemiologi klinis (*Clinical Epidemiology* - CE) dan *Evidence-based Medicine* (EBM) telah menjadi bagian penting kurikulum pendidikan kedokteran di seluruh dunia. Pada **bab 6**, diuraikan mengenai proses adaptasi dan penyelenggaraan modul pembelajaran terintegrasi CE dan EBM di Fakultas Kedokteran Universitas Indonesia (UI), Jakarta dan di University of Malaya (UM), Kuala Lumpur. Modul disusun dan telah dilaksanakan di University Medical Center Utrecht (UMCU) sebelumnya. Sebelum modul dimulai, staf pengajar UI dan UM mengikuti *training of teachers* (TOT). TOT diterima dengan baik oleh staf pengajar UI dan UI, dan setelah diadaptasi, modul CE dan EBM kemudian diselenggarakan di kedua fakultas kedokteran. Hasil pre-test mahasiswa UI dan UM secara bermakna lebih rendah dari mahasiswa UMCU ($p<0.001$). Hasil post-test mahasiswa UMCU sebanding ($p=0.48$) dengan UI, namun berbeda secara bermakna ($p<0.001$) dengan mahasiswa UM. Masalah yang sama-sama dilaporkan di UI dan UM adalah akses terhadap literatur kedokteran yang terbatas dan terdapatnya variasi pada kemampuan tutor. Disimpulkan bahwa adopsi dan integrasi modul pembelajaran CE-EBM yang berasal dari negara barat ke fakultas kedokteran di Asia dapat dilaksanakan dan mencapai hasil pembelajaran mahasiswa yang setara.

Efek jangka pendek langsung modul *Clinical Epidemiology* dan *Evidence-based Medicine* (CE-EBM) terhadap pengetahuan, sikap dan perilaku

mahasiswa kedokteran di University Medical Center Utrecht (UMCU), Universitas Indonesia (UI) and University of Malaya (UM) diuraikan di **bab 7**. Pada pengukuran tersebut, digunakan versi adaptasi suatu kuesioner yang terdiri atas 26 item yang terbagi atas 4 sub-skala: pengetahuan, sikap, perilaku dan penggunaan lanjut *Evidence-based Practice* (EBP). Secara keseluruhan terdapat 526 mahasiswa (224 UI, 202 UM dan 100 UMCU) yang mengisi kuesioner. Di ketiga fakultas kedokteran, nilai Cronbach's alpha total skor kuesioner dan ke-4 sub-skala selalu melebihi 0.6. Mahasiswa UMCU memperoleh skor pra-modul tertinggi di semua sub-skala dibandingkan mahasiswa UI dan UM. Modul CE-EBM secara bermakna ($p<0.001$) meningkatkan pengetahuan mahasiswa UMCU dan UM namun tidak pada mahasiswa UI. Skor sikap pasca modul di ketiga fakultas kedokteran tidak berubah secara bermakna sehingga disimpulkan bahwa pembelajaran EBP secara langsung berefek pada pengetahuan namun tidak pada sikap. Perbedaan skor pra-modul kemungkinan diakibatkan oleh perbedaan sistem, infrastruktur dan kurikulum pemebelajaran ketiga fakultas kedokteran.

Pada **bab 8** kami menyampaikan argumen bahwa *Evidence-based Practice* (EBP) sangat penting pada situasi dimana terdapat permasalahan kesehatan yang besar dan berat dimana sumber daya yang terbatas perlu dimanfaatkan seefektif mungkin. Walaupun konsep EBP berasal dari negara maju, penerapannya di negara berkembang seperti Indonesia sangatlah relevan. Walaupun perkembangan penguasaan pengetahuan dan keterampilan EBP di Indonesia cukup menggembirakan, namun dibutuhkan penerapan hal tersebut dalam rangka menyelesaikan permasalahan kesehatan Indonesia. Upaya mengintegrasikan EBP pada praktik klinis sehari-hari ("*knowledge translation*") merupakan isu penting saat ini. Pada bab-bab sebelumnya telah diidentifikasi berbagai kesenjangan pada produksi dan pemanfaatan pengetahuan terutama terkait penatalaksanaan diabetes. Kesenjangan produksi pengetahuan meliputi terbatas dan rendahnya kualitas bukti

terkait penatalaksanaan diabetes, sedikitnya jumlah *systematic review* terkait penatalaksanaan diabetes yang relevan dengan situasi Indonesia dan rendahnya kualitas penyusunan dan kemampu-terapan (*applicability*) panduan praktik klinis diabetes yang saat ini ada di Indonesia. Berdasarkan penggunaan model "*awareness to adherence*" diketahui bahwa tingkat pengetahuan (*awareness*) yang tinggi diikuti oleh rendahnya tingkat persetujuan (*agreement*), adopsi (*adoption*) dan kepatuhan (*adherence*). Kesenjangan yang ditemukan harus dianalisis lebih mendalam secara cermat dengan melibatkan pengandil (*stakeholders*) terkait. Upaya tersebut juga harus diikuti oleh penerapan siklus "*action"* pada proses translasi bukti ilmiah (*knowledge translation).* Sebagai kesimpulan akhir, upaya peningkatan kapasitas dalam EBP harus dilakukan bersamaan dengan upaya mendorong proses translasi bukti ilmiah dalam rangka mencapai peningkatan pelayanan kesehatan di negara berkembang seperti Indonesia.

Appendix

An Asia-Europe collaboration in Clinical Epidemiology and Evidence-based Medicine

Indah S. Widyahening[1,2]

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Background

While Evidence-based Medicine emerged in the 1990's from Canada and the UK, interest has rapidly spread around the world. However, lack of adequate staff and training in the practice and teaching of clinical epidemiology and EBM has been a limiting factor. Hence national capacity development is vital if the principles of EBM are to spread. One example is the AsiaLink project.

In November 2007 the Asia-link project in Clinical Epidemiology and Evidence-based Medicine (CE & EBM) was funded by the European Commission to build competences and capacity in clinical epidemiology and Evidence-based Medicine in Indonesia and Malaysia. The aim was developing durable improvement in CE & EBM teaching and research in Indonesia and Malaysia.

The project intensified collaboration and exchange of researchers between Europe and Asia. The partners were Cipto Mangunkusumo Hospital – Faculty of Medicine University of Indonesia, University of Malaya (Malaysia), Julius Center at the University Medical Center Utrecht (the Netherlands) and the Center of Evidence-based Medicine at Oxford University (UK), with a Steering committee of Yolanda van der Graaf, Arno Hoes, Diederick Grobbee and Helena Verkooijen from Utrecht, Paul Glasziou from Oxford, Awang Bulgiba from Malaysia and Sudigdo Sastroasmoro from Indonesia.

To achieve the above aims, the three main activities were:

- Conduct CE & EBM courses and teaching program at both undergraduate and post-graduate level at the University of Indonesia in Jakarta and the University of Malaya in Kuala Lumpur,
- Establish a collaborative PhD fellowship program, to develop core staff with solid post-graduate training in CE and EBM,
- Establish two regional CE&EBM support units: at the University of Indonesia in Jakarta and the University of Malaya in Kuala Lumpur.

CE & EBM postgraduate courses

By the project's end in November 2010, over 20 post-graduate CE & EBM courses have been conducted, with over 500 participants. While these courses were initially led by staff members from Utrecht and Oxford, as planned, UI and UM staff members gradually took over. To improve their EBM teaching. several staff members from University of Indonesia and University of Malaya also attended the 3-day and 5-day EBM workshops in Oxford, initially as course participants and at later stages as facilitators.

CE & EBM undergraduate teaching program

In 2009, a CE-EBM module was successfully implemented for undergraduate students in Indonesia and Malaysia. This module was designed and implemented in Utrecht since 2004 and originally ran as two separate CE (6 weeks) and EBM (5 weeks) modules. This module was adapted to fit the medical curricula of the University of Indonesia and University of Malaya. In responds to local needs, the module in UI was given as a four-week CE-EBM module to the 4th year students, while in UM this module was integrated to the Social and Preventive Medicine module which was given to 3rd year medical students for four months. Prior to implementing the module, a three days Training of Teachers (TOT) course was given at University of Indonesia and University of Malaya. These TOT courses were led by the module developers from Utrecht: Geert van der Heijden and Maroeska Rovers.

PhD fellowship program

Ten PhD fellows, six from University of Indonesia and four from University of Malaya, were given opportunity to deepen their knowledge and expertise in specialized areas of clinical epidemiology on an international level. Nine fellowships were carry-out in Utrecht and one in Oxford. All of them were

also actively involved during teaching activities in post-graduate courses and undergraduate modules. All these PhD projects will be completed by the end of 2011.

Regional CE&EBM support units

In May 2009 the Julius Center University of Malaya (JCUM) was established. This CE & EBM unit aims to facilitate regional CE & EBM educational and research activities and promote collaboration between Asia and Europe in the area of CE & EBM. In September 2010 the CE & EBM Center at the Faculty of Medicine University of Indonesia – Cipto Mangunkusumo Hospital in Jakarta was officially opened in the presence of the Minister of Health and the EU Ambassador.

Closing Conference

The international conference "Clinical Epidemiology and Evidence-based Medicine in global perspective" on 27 and 28 November 2010 held in Kuta, Bali, Indonesia, marked the formal closing of the project. Approximately 320 attendees from 11 countries participated in the conference which indicates

the growing interest on CE & EBM in Asia. This conference comprised six parallel courses and workshops including basic clinical epidemiology, introduction to EBM, clinical trials, systematic reviews, teaching EBM, and infectious diseases epidemiology and vaccine development. Several experts with international reputation in this area including Paul Glasziou from Bond University (Queensland, Australia) and Oxford University (UK), Arno Hoes and Diederick Grobbee from Utrecht University and Chia Kee Seng from the National University of Singapore were present to share their knowledge.

Continuation of Collaboration

In order to strengthen and stabilize CE & EBM research and teaching resulting from this Asialink CE & EBM project, Cuno Uiterwaal currently holds a visiting professorship both at University of Malaya. (October-November 2010) then University of Indonesia (December 2010-January 2011). The collaboration established during this Asialink CE & EBM project will be maintained through joint projects.

Some important lessons from this 3-year project were:

- Flexibility and adaptation are vital: courses must be adapted to fit the needs and structures of the local environment,
- An early, but staged, transfer of teaching skills is essential: local teachers need to be identified and learn in stages to take over the undergraduate and postgraduate teaching,
- Start a PhD program early: a core of PhD trained staff are needed for the leadership roles in CE and EBM.

Colloquially these lessons might be summed up by the sayings: “Adapt to adopt” and “The best time to plant a tree is 20 years ago, the second best time is today”.

For more information: www.asialink-ce.org

Publications and Awards

Manuscript presented in this thesis

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Publications and awards related to this thesis

Presentations

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Widyahening IS. Teaching Evidence-based Practice to medical students; the use of Evidence-based Case Report. Oral presentation. 18th WONCA Asia Pacific Regional Conference, Cebu, Philippines, 21-24 February 2011.

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Awards

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International Scientific Publication Award 2016 from the Indonesia Endowment Fund for Education

Widyahening IS, van der Graaf Y, Soewondo P, Glasziou P, van der Heijden G. Awareness, agreement, adoption and adherence to type 2 diabetes mellitus guidelines: a survey of Indonesian primary care physicians. BMC Family Practice 2014, 15:72

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About the Author

Indah Suci Widyahening obtained her medical doctor (MD) degree from the Faculty of Medicine Universitas Indonesia (FKUI), Jakarta in 1997. She then continued her study in the Postgraduate Program in Occupational Health and Safety of the Universitas Indonesia and obtained her MSc in 2000 with the thesis on the mental-emotional disturbances among airline pilots. Shortly after that, she began to work as an academic staff in the Community Medicine Department of FKUI. In 2001, she received a scholarship from the Asian Development Bank to obtain an MSc in the Clinical Medicine – Family Medicine from the College of Medicine University of the Philippines in Manila which she completed in 2002.

During her MSc program in Manila, she was firstly introduced to Evidence-based Medicine and became fascinated to it ever since. Her thesis is about teaching literature search for the medical students when she initiated a literature search workshop to the FKUI final year medical students during community medicine rotation.

Under the Asialink Clinical Epidemiology and Evidence-based Medicine collaboration, she was given the opportunity to participate in the workshops on Teaching Evidence-based Practice in Oxford Centre for Evidence-based Medicine, first as a participant and then a facilitator. She has also been appointed as the Clinical Epidemiology and Evidence-based Medicine (CE-EBM) module coordinator of FKUI since 2009 which became the basis of her PhD research.

Besides her teaching activities, she is also a primary care physician who held a responsibility as the head of two Family Medicine Clinics of the FKUI alternately since 2002; a position she had to let go when she started her PhD program in the Julius Center of Health Sciences and Primary Care University Medical Center Utrecht early in 2010.

Currently, she is the research coordinator of the Community Medicine Department of the FKUI. On the national level, she is a member of the National Board for the Enhancement of the Primary Care Physicians Education in Indonesia whose main task is to prepare a nation-wide post-graduate education for primary care physicians and the secretary of the National Colleagues of the Primary Care Physicians. She is also a member of the National Experts Committee on the Control of Non-communicable Diseases in Indonesia.

Her other key interest is on diabetes research. She managed several nation-wide projects on diabetes care in collaboration with the Indonesian Society of Endocrinology, the Indonesian Diabetes Association, the Indonesian Pediatric Society, the Ministry of Health and the World Diabetes Foundation; a role which enables her to do her other passion which is travelling.