Journal of the ASEAN Federation of Endocrine Societies

ORIGINAL ARTICLE

Development of a Validated Diabetes Risk Chart as a Simple Tool to Predict the Onset of Diabetes in Bogor, Indonesia

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Abstract

Objective. To develop a simple, non-invasive tool for predicting the onset of type 2 diabetes mellitus (T2DM).

Methodology. A total of 4418 nondiabetic respondents living in Bogor were included in this cohort study. Their ages ranged from 25 to 60 years old and were followed for 6 years with interviews, physical examinations and laboratory tests. The investigators used logistic regression to create a tool for diabetes risk determination.

Results. The cumulative incidence of T2DM was 17.9%. Risk factors significantly associated with T2DM included age, obesity, central obesity, hypertension and lack of physical activity. The Bogor Diabetes Risk Prediction (BDRP) chart had a cut-off of 0.128, with sensitivity of 76.6% and specificity of 50.3%. The Positive Predictive Value (PPV) was 21.6% and Negative Predictive Value (NPV) was 92.3%. The Area under the Curve (AUC) was 0.70 with a 95% confidence interval ranging from 0.675-0.721.

Conclusion. The BDRP chart is a simple and non-invasive tool to predict T2DM. In addition, the BDRP chart is reliable and can be easily used in primary health care.

Key words: diabetes screening, risk factors, diabetes, cohort study, Bogor

INTRODUCTION

Diabetes Mellitus (DM) is an increasingly prevalent global chronic disease that can have serious complications. Data from the International Diabetes Federation (IDF) shows that Indonesia is among the top 10 countries with the highest prevalence of DM among individuals aged 20 to 79 years. In 2019, it was projected that the number of patients with diabetes would increase from 10.7 to 13.7 million by 2030.[1] In a nationwide community-based survey known as RISKESDAS conducted under the Ministry of Health of the Republic of Indonesia, the diabetes prevalence in individuals younger than 15 years old was noted to continue to increase every year. RISKESDAS (2018) showed that the cases of undiagnosed Diabetes Mellitus (UDD) increased from 6.9% in 2013 to 8.5% in 2018. On the other hand, diagnosed Diabetes (DD) cases increased from 1.5% in 2013 to 2.0 % in 2018. Noticeably, the prevalence of UDD was higher than that of DD.[2-4]

The increasing incidence of diabetes must be curtailed since the subsequent development of micro- and macrovascular events is a socioeconomic burden on the patient's family. Risk factor control and early T2DM detection are crucial to reduce diabetes complication rates. In addition, counseling with regard to self-assessment of diabetes risk is important to raise public awareness about their health conditions. Models for diabetes risk assessment have been developed in several countries mostly in America, Europe and China through cross-sectional or cohort studies that used questionnaires and blood tests.[5,6]

There are fewer studies from Korea, Hong Kong and Thailand, with observation times ranging from 4 to 12 years. The results indicate that the risk factors for T2DM are generally similar across the different ethnic groups with age, family history of DM, obesity and hypertension as the most common.[7,8]

Some studies, included other variables depending on the conditions of the country or region. The Finnish FINRISK study, included these additional variables: antihypertensive drug intake, antidiabetic drug intake and consumption of fruits and vegetables.[9] Furthermore, a study from Korea included smoking and HbA1c levels as risk variables; while a study in Zhanang (China) included

ISSN 0857-1074 (Print) | eISSN 2308-118x (Online)
Printed in the Philippines

Received: August 30, 2021. Accepted: November 30, 2021.
Published online first: April 27, 2022.
https://doi.org/10.15605/jafes.037.01.09

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frequent tea-drinking habits, hypertriglyceridemia and fasting plasma glucose (FPG).[7,10] Subsequently, excess meat consumption was found to be a risk factor in a study in Daqiang, China, while total sleep time and waist circumference were included in other studies. Non-invasive models from these risk factors showed a fair value with means an AUC of 0.7-0.8 for predicted diabetes.[11,12]

Similar studies among Indonesians are rare. Hence, we developed a simple and non-invasive diabetes risk prediction model based on the data obtained from the Bogor Cohort Study of the Risk Factors of Non-Communicable Diseases (BCSRFNCD).[7,10-12] The result of this prediction model is presented in chart form to make it easier to apply in the community. Utilizing this model, we aim to develop a screening tool for the prediction of T2DM among adults in Indonesia, and that this self-assessment tool can be used to determine the risk of developing T2DM in the community.

METHODOLOGY

Participants

This analysis is part of the BCSRFNCD that was conducted by the National Institute of Health Research and Development (NIHRD) under the Ministry of Health of the Republic of Indonesia in 5 villages located in the Central Bogor District, Bogor City. Subject recruitment took place in three stages in 2011, 2012,and 2015. A total of 5690 respondents aged 25-60 years were included and were followed biennially for six years. A total of 4418 non-diabetic stage 1 and 2 subjects were eventually enrolled and underwent complete laboratory examination.

The reasons for failure to follow-up (dropout) included pregnancy, change of residence, and work-related. Figure 1 illustrates the methodology flow chart.

Ethics committee approval

This research was approved by the Ethics Commission of the National Institute of Health Research and Development (NIHRD).

Interview and physical examination

Data were collected using the WHO STEPS method. Informed consent was obtained before blood sampling. Interviews were conducted to determine each patient's sociodemographic characteristics, diagnoses, symptoms and efforts to prevent and treat diabetes.[12] Trained health workers measured the subjects' body weight, height, abdominal circumference and blood pressure using standardized tools.

According to the recommendation of the MHRI, obesity was defined as a body mass index (BMI) ≥25.0 kg/m^2. Abdominal circumference ≥90 cm in men or ≥80 cm in women was categorized as central obesity. Abdominal circumference was obtained by placing a measuring-tape around the most prominent part of the abdomen, which is usually located midway between the lower ribs and the iliac crests. Respondents were asked to wear light clothes and stand straight with their feet together. Hypertension was determined based on a history of antihypertensive drug intake, a measured systolic blood pressure ≥140 mmHg, and/or a diastolic blood pressure ≥90 mmHg. Blood pressure measurement with a digital sphygmomanometer was performed while the individual was in a sitting position with the cuff placed on the right arm at the level of the heart. Blood pressure measurement was carried out twice within approximately 3 minutes. If there was a difference of greater than 10 mmHg between the two measurements in both the systolic and diastolic pressure, it was retaken after a 10-minute rest.[13]

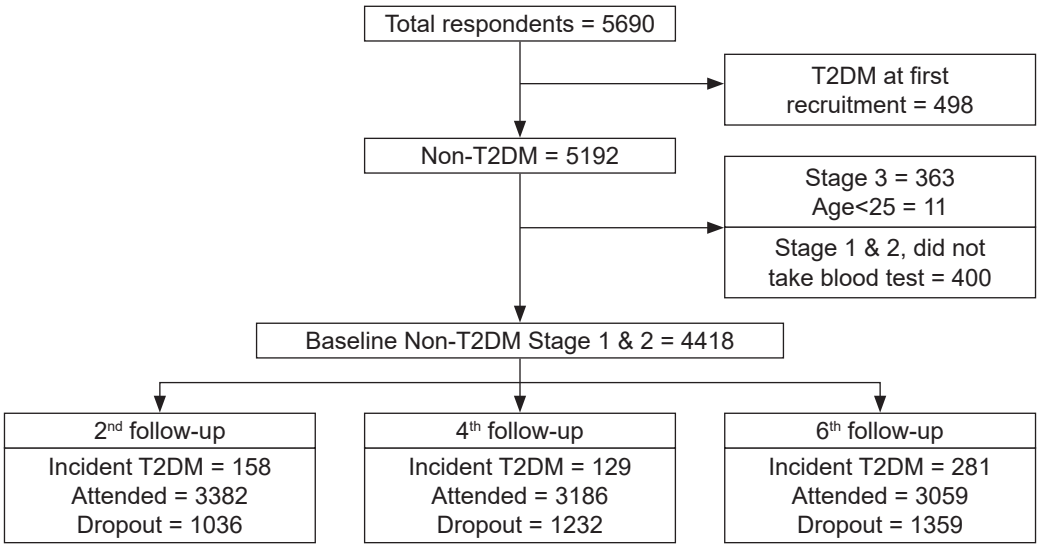

Figure 1. The flow of determining respondents of The Bogor Cohort Study of the Risk Factors of Non-Communicable Diseases (BCSRFNCD).

Laboratory examination

Approximately 8 ml of venous blood was taken from each respondent after a 10- to 12-hour fast for analysis of the fasting plasma glucose (FPG) and lipid profile which includes total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL) and triglycerides. Blood extractions were carried out at the Bogor "cohort house" by experienced laboratory personnel. After samples for fasting blood sugar were obtained, the respondents were given a drink containing 75 grams of glucose. Blood samples for glucose (~ 3ml) were taken 2 hours after the glucose load. FPG and 2-hour 75-g oral glucose tolerance test (OGTT) were measured using the glucose hexokinase II (GLUH) method. Total cholesterol was measured enzymatically. Serum LDL and HDL were measured using the homogeneous method. Serum triglycerides were measured using the glycerol-3-phosphate oxidase (GPO) method. The following blood results were considered as abnormal: total cholesterol ≥200 mg/dl, triglycerides ≥150 mg/dl, LDL ≥100 mg/dl, HDL ≤40 mg/dl in men and ≤50 mg/dl in women.[13]

A diagnosis of diabetes was given if the subject fulfilled the American Diabetes Association (ADA) criteria (FPG ≥126 mg/dl, 2-hour 75-g OGTT ≥200 mg/dl).[14,15] Respondents were further classified as either "Diagnosed Diabetes Mellitus" (DDM) if they were previously diagnosed by a physician, or "Undiagnosed Diabetes Mellitus" (UDD) if they were not previously diagnosed.

Statistical analyses

Data analyses were carried out in stages including data exploration (univariate), simple relationship analysis (bivariate), and multivariable. Logistic regression was used in multivariate analysis to assess the relationship between risk factors and the incidence of T2DM and eventual modeling. Variables that had a *p*-value of less than 0.25 in the bivariate analysis were included in the multivariate analysis to obtain the results of the T2DM risk-fit model. Cut-off point, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and area under the curve (AUC) using the receiver operating curve (ROC) graph were also determined. Plasma glucose results served as the reference standard for the diagnosis of diabetes (ADA criteria).[16–18]

The predictive finest cut-off value of BCSFRNCD was compared with the ADA questionnaire scoring in the same population. The ADA questionnaire was chosen because it has been widely used in many countries and has proved to be useful. In the ADA questionnaire, age was categorized into four groups: 25-39, 40-49, 50-59, and ≥60 years old. SPSS v.21 (IBM, New York, Chicago) was used for the analyses.

RESULTS

Majority of the 4418 respondents were women between the ages of 25 and 39 years. Only 13.9% of the respondents had a family history of diabetes. Based on BMI, 50% of the respondents were obese. The majority of respondents did not have central obesity or hypertension. Most of the respondents have high total cholesterol and LDL levels. Regarding glucose status, 5.3% had impaired fasting glucose (IFG), while 21.6% had impaired glucose tolerance (IGT). On the second year, 158 out of 3382 respondents who followed-up were diagnosed with DM. On the fourth year, 129 out of 3186 returning respondents developed DM. On the sixth year, 281 out of the 3059 subjects developed DM. Within 2 to 6 years of follow-up, the proportion of the cohort with hypertension, obesity, central obesity, hypercholesterolemia and hypertriglyceridemia increased. The cumulative 6-year incidence of T2DM in the 5 villages of Central Bogor was 17.9 % (n = 568), with majority having UDD as shown in Table 1.

The results of the multivariate analysis showed that age, obesity, hypertension, central obesity and lack of physical activity increased the risk of developing T2DM (Table 2). A cut-off point of the Bogor Diabetes Risk Prediction (BDRP) was obtained using the ROC graph with cumulative incidence of DM (on year 6) as the dependent variable and plasma glucose levels as the reference standard. Using a cut-off point of 0.128, the risk prediction model has a sensitivity of 76.6%, specificity of 50.3%, PPV of 21.6%, and NPV of 92.3%. The AUC was 0.70 (95% confidence interval 0.675-0.721). The accuracy of the BDRP in predicting T2DM compares favorably with the ADA questionnaire which has a sensitivity of 70.4%, specificity of 58.5%, PPV of 20.0%, NPV of 93.0%, and AUC of 0.70 (Figure 2).

After data analysis, the identified risk factors for diabetes were converted into a chart called the BDRP Chart as shown in Figure 3. At a cut-off point of 0.128, the probabilities of developing T2DM among those above 60 years old and those 50-59 years old were similar, hence, they were combined into one chart. The presence of 2 or more risk factors in a respondent who is at least 46 years old

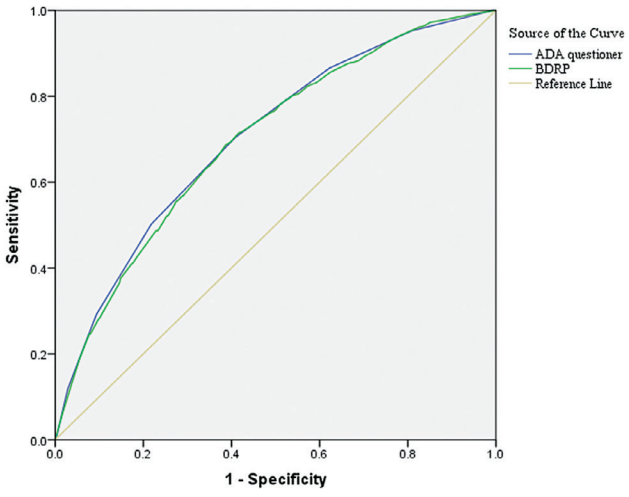

Figure 2. ROC analysis of the BDRP and the ADA questioner of The Bogor Cohort Study of the Risk Factors of Non-Communicable Diseases (BCSRFNCD) respondents.

Table 1. Characteristics of non-T2DM respondents in the Cohort Study Risk Factors of NCDs

Characteristics	baseline (n=4418)		2nd FU (n=3382)		4th FU (n=3186)		6th FU (n=3059)	
	n	%	n	%	n	%	n	%
Gender								
Men	1548	35	1030	30.5	942	29.6	889	29.1
Women	2870	65	2352	69.5	2244	70.4	2170	70.9
Age								
25-39	1655	37.5	982	29.0	730	22.9	555	18.1
40-49	1402	31.7	1137	33.6	1082	34.0	976	31.9
50-59	1063	24.0	920	27.2	926	29.1	939	30.7
≥60	298	6.7	343	10.1	448	14.1	589	19.3
Family history of diabetes								
No	3804	86.1	2643	78.1	2463	77.3	2380	77.8
Yes	614	13.9	739	21.9	723	22.7	679	22.2
Hypertension*								
No	3134	70.9	2376	70.3	2270	71.2	1905	62.3
Yes	1284	29.1	1006	29.7	916	28.8	1154	37.7
Obese**								
No	2471	55.9	1677	49.6	1535	48.2	1370	44.8
Yes	1947	44.1	1706	50.4	1649	51.8	1687	55.2
Central obesity***								
No	2663	60.3	1675	49.9	1361	41.3	1139	37.3
Yes	1755	39.7	1685	50.1	1868	58.7	1918	62.7
Physical activity****								
appropriate	2265	51.3	1330	39.3	1718	53.9	2082	68.1
not appropriate	2153	48.7	2052	60.7	1468	46.1	977	31.9
Total Cholesterol*****								
Normal	2238	50.7	1862	55.1	1589	49.9	1160	38.1
Risk	2180	49.3	1520	44.9	1597	50.1	1886	61.9
LDL-chol*****								
Normal	781	17.7	613	18.1	582	18.3	489	16.1
Risk	3637	82.3	2769	81.9	2604	81.7	2557	83.7
HDL-chol*****								
Normal	2688	60.8	2074	61.3	2124	66.7	1755	57.4
Risk	1730	39.2	1308	38.7	1062	33.3	1304	42.6
Triglycerides*****								
Normal	3657	82.8	2749	81.3	2552	80.1	2271	74.2
Risk	761	17.2	633	18.7	634	19.9	788	25.8
T2DM******								
No	4418	100.0	3224	95.3	3057	96.0	2778	90.8
Yes			158	4.7	129	4.0	281	9.2
-DDM			29	18.4	34	26.4	12	4.3
-UDD			129	81.6	95	73.6	269	95.7

*Hypertensive: if systolic ≥140 mmHg and/or diastolic ≥90 mmHg (JNC VII)
**Obese: BMI ≥25 kg/m^2
***Central obesity: if the abdominal circumference is ≥90 cm (men), ≥80 cm (women)
****inadequate physical activity: if <600 Meq
*****Risk of total cholesterol ≥200 mg/dL, triglycerides ≥150 mg/dL, LDL ≥100 mg/dL, HDL ≤40 mg/dL (men) and ≤50 mg / dL (women).
******T2DM: if FPG ≥126 mg/dL or post 75g-OGTT ≥200 mg/dL (ADA criteria)

predicts T2DM. Among respondents between 25-39 years old, having 3 risk factors was predictive of T2DM. In contrast, having only one risk factor was not predictive with a sensitivity of 76.6%.

DISCUSSION

The 6-year cumulative incidence of T2DM in the 5 sub-districts of Bogor City was quite high at 17.9% and prevalence 23.4% (include diabetes patients at baseline). This is very concerning since the majority of the population (70 to 95%) did not realize that their blood glucose levels were high (UDD). This is considerably higher compared to the national diabetes prevalence of 8.5% and the West Java Province prevalence from RISKESDAS result of 2.05%.[3,4] This finding is similar to a Thai study which revealed that 13.5% of 2,677 respondents in the 35–55 age group had T2DM after a 12-year follow-up.[19] An Israeli study showed that 13.7 % of the 1,894 respondents in an Arab community aged 21 years and above had T2DM.[8] This result was lower than the study in Saudi Arabia, where 25.1% of the 872 respondents had T2DM.[20] Thus, the increasing prevalence of T2DM, particularly UDD, requires more intensive prevention efforts by early identification of the risk factors. Furthermore, it is necessary to increase public awareness and to conduct self-assessment of diabetes risk routinely.

Risk factors that predicted the occurrence of T2DM among the respondents of the Bogor Cohort Study were age, obesity, central obesity, hypertension, and lack of physical activity. The BDRP model had a fairly good sensitivity, specificity and AUC. Furthermore, monitoring of bodyweight, abdominal circumference, blood pressure, and physical activity is easy to carry out in the community.

Table 2. The result of the multivariate analysis for T2DM prediction for the Cohort Study Risk Factors of NCDs

Variables	β	p	RR	CI 95%	
				lower	upper
Age group					
25-39	-	-	ref	-	-
40-49	0.393	0.013	1.481	1.088	2.016
50-59	0.662	0.001	1.940	1.435	2.622
≥60	0.816	0.001	2.261	1.635	3.126
Obese**					
No	-	-	ref	-	-
Yes	0.600	0.001	1.822	1.402	2.368
Hypertensive*					
No	-	-	ref	-	-
Risk	0.574	0.001	1.775	1.466	2.148
Central obesity***					
No	-	-	ref	-	-
Yes	0.518	0.001	1.679	1.272	2.215
Physical activity****					
No	-	-	ref	-	-
Risk	0.459	0.001	1.582	1.310	1.909
Constant	-3.388	0.001	-	-	-

*Hypertensive: if systolic ≥140 mmHg and/or diastolic ≥90 mmHg (JNC VII)
**Obese: if BMI ≥25 kg/m^2
***Central obesity: if abdominal circumference ≥90 cm (in men), ≥80 cm (in women)
**** inadequate physical activity: if <600 Meq

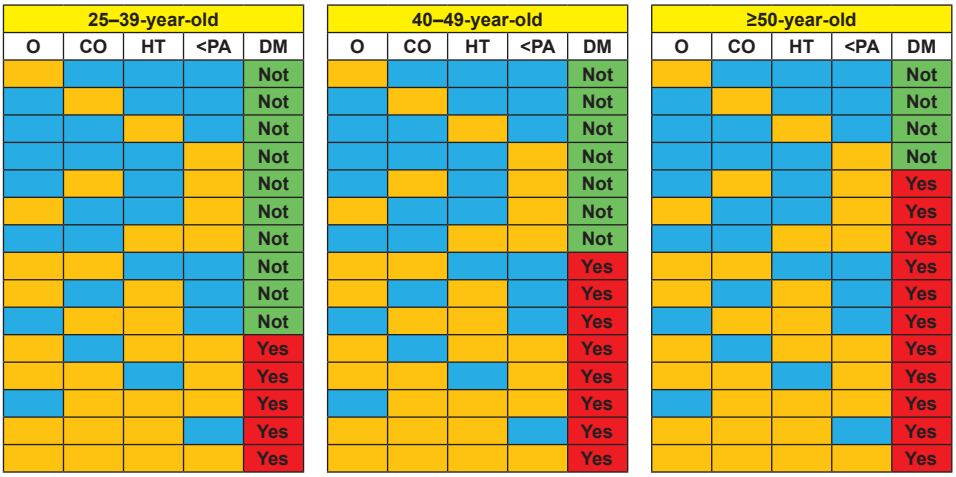

Figure 3. The Bogor Diabetes Risk Prediction (BDRP) Chart.

The Ministry of Health has an Integrated Services Post for Non-Communicable Diseases (NCD) program called "*Posbindu*" that performs these checks every month and records the results in the NCD Cohort Book for each individual. The development of the BDRP Chart from the BDRP model aims to simplify interpretation, with the hope that it can be used for T2DM self-assessment and screening. Compared to other studies with scoring systems, this chart differs in the prediction of T2DM. However, researches in America, Australia, Europe and Asia have almost the same variables.

Similar to our findings, various studies in America also showed that age, gender, family history of diabetes mellitus, history of hypertension, obesity and physical activity are risk factors for diabetes.[21] An Australian study showed that the risk factors for T2DM are a history of high plasma glucose, antihypertensive drug intake, and smoking.[22] Age, gender, history of high plasma glucose, antihypertensive drug intake, obesity, central obesity, physical activity, and fruit and vegetable consumption were included in the prediction models from studies conducted in Finland and Denmark.[9,23] Cross-sectional studies among Israeli-Arabs, Saudi Arabians, Indians, Omanis and Thais show that age, family history of diabetes, obesity, central obesity and physical activity are all associated with T2DM.[8-21,24] Hypertriglyceridemia and high FPG were shown to predict T2DM occurrence in a 6-year prospective cohort study in China.[10] This finding was attributed to the frequent intake of tea. The difference in the variables included in this predictive model could be due to variations in habits such as diet.

The BDRP Chart had a higher sensitivity but lower specificity compared to the results of a cohort study in China which had a sensitivity of 69,63%, specificity of 75.56% and AUC of 0.791.[10] Our results are nearly identical to the Thai cohort which had a sensitivity of 77%, specificity of 60%, and AUC of 0.74.[19] These results were better than other Chinese studies among respondents aged 20-74 years old, which showed an AUC of 67.3 % at 95 % CI (64.9-69.7).[25] Similar with research in India from the Chennai Urban Rural Epidemiology Study (CURES) used the Indian Diabetic Risk Score (IDRS) and obtained an AUC of 0.698 using 95% CI ranging from 0.663-0.733.[26]

The BDRP chart was compared to the ADA risk score questionnaire which is widely used in many countries.[27] Results showed that the BDRP had diagnostic values that are nearly identical to the ADA questionnaire. A tool with high sensitivity can be used as a screening tool. The BCSFRNCD respondents found it easier to provide data using the BDRP chart than the ADA questionnaire because, particularly for those living in urban communities, most were unable to provide an accurate information regarding their family history. The majority of the respondents were immigrants who did not live close to their parents, hence, they are uncertain of their health status. Moreover, since medical records have not yet been integrated into a single health system, recording of the health history of the Indonesian population has not been properly implemented. In addition, the colours displayed on the BDRP chart are easier to understand.

Without question, this chart can be applied to Indonesian women. The lack of knowledge about gestational diabetes among Indonesian women is difficult to overcome due to lack of public awareness, and limited knowledge of pregnant women about the management of gestational diabetes.[28]

Limitations of the study

The multivariate analysis uses only non-invasive risk factors variables. The study population has fewer male than female respondents and, hence, may not reflect the general population of Bogor. Further validation in a larger population is warranted.

CONCLUSION

The cumulative incidence of T2DM in Bogor is 17.9%. The risk factors that predict its occurrence are age, obesity, central obesity, hypertension and lack of physical activity. The BDRP Chart fared well when compared to the ADA questionnaire in terms of predicting who will develop T2DM among the BCSRFNCD population. The BDRP Chart is a simple, non-invasive and easy-to-use screening tool that can be employed in "*Posbindu*" and primary healthcare. Moreover, the BDRP chart colour stresses the importance of adopting a healthy lifestyle.

Acknowledgments
The authors thank the Head of the Bogor City Health Office as well as the staff, doctors and officers of Puskesmas Belong, Merdeka, and Sempur; cadres in Babakan, Babakan Pasar, and Kebon Kalapa villages, the respondents who volunteered to participate in the research, and everyone who has supported this research.

Statement of Authorship
All authors certified fulfillment of ICMJE authorship criteria.

Author Disclosure
The authors declared no conflict of interest.

Funding Source
The study was funded by the National Institute of Health Research and Development, Ministry of Health of Republic of Indonesia (no award/grant number).

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