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Metabolic Syndrome as a Predictor of Incident Chronic Disease in Middle-Aged Chinese Persons

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Abstract

Background: Rising incidence of chronic diseases is a global phenomenon responsible for the greatest increase in burden of disease. **Objective:** To determine the prevalence of the metabolic syndrome (MetS) in a sample of middle-aged Chinese individuals and the onset of incident diabetes, hypertension, and hyperlipidemia in the ensuing 4 years. **Subjects:** 638 men and women born in 1956, 1960–1961, and 1964 in Yuci, Shanxi Province, China, were voluntarily enrolled. **Method:** Longitudinal study collecting anthropometric measures, blood chemistry, behavioral information, and disease information by survey, in 2008 and 2012 in the community health centers of Yuci, China. Data were analyzed using descriptive measures and regression analysis. **Results:** The rate of MetS in 2008 was 50.95% and 37.15% for men and women ($p = 0.001$) and in 2012 was 49.52% and 46.26% for men and women ($p = 0.438$). Regression analysis of the ability of MetS in 2008 to predict disease in 2012 resulted in odds ratios of 2.51 (1.43, 4.41), 26.82 (3.46, 207.68), and 4.06 (2.41, 6.86), for hypertension, diabetes, and hyperlipidemia. **Conclusion:** MetS has potential as a screening tool to predict incident chronic disease and to aid in improved primary disease prevention.

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Secondary data analysis: The Metabolic Syndrome study data set is available for secondary data analysis from the corresponding author by request.

Keywords

diabetes; preventive medicine; cardiovascular disease; obesity

Metabolic syndrome (MetS) is a concept used in health promotion to describe a cluster of risk factors that have been shown to identify individuals at high risk for eventual cardiovascular disease (CVD) or impaired glucose tolerance (Goldenberg & Punthakee, 2013). The risk factors include elevated waist circumference, elevated triglycerides (TG), reduced high-density lipoproteins (HDL), elevated blood pressure, and elevated fasting plasma glucose. MetS affects 20–30% of the population of developed countries (AlSaraj et al., 2009) and is associated with a significant risk of CVD and type 2 diabetes, especially in men over age 45 and women over age 55 (Lorenzo, Williams, Hunt, & Haffner, 2007). With increased economic prosperity in China has come a more sedentary lifestyle and a higher caloric intake, and chronic diseases now account for 80% of all deaths in China (Wang, Kong, Wu, Bai, & Burton, 2005), having increased significantly in recent years (Yang et al., 2012).

The development of diabetes and CVD in a population represents multiple routes of progression, depending on the start point and the pattern of development over time (Vistisen et al., 2014). Therefore, the longitudinal method used in this study allows for elucidation of the progression of MetS by describing the sequential appearance of the individual components of MetS. The theoretical perspective underlying this research is that as Chinese populations experience increased prosperity over time, MetS onset will begin earlier, and that the presence of MetS will predict the onset of hypertension, diabetes, and hyperlipidemia (Bragg et al., 2016). This creates the opportunity to compress the duration of morbidity by intervening in those people with MetS to prevent or delay the onset of disease (Andersen, Sebastiani, Dworkis, Feldman, & Perls, 2012).

This longitudinal study was designed to answer the question of whether the presence of MetS was able to predict new onset cases of hypertension, diabetes, or hyperlipidemia 4 years later. Our specific aims in this study were to

1. determine whether the presence of MetS in 2008 would significantly predict the likelihood of developing hypertension, diabetes, or hyperlipidemia in 2012;
2. compare prevalence of hypertension, diabetes, hyperlipidemia, and MetS between men and women from 2008–2012; and
3. explain which components lead to the presentation of hypertension, diabetes, and hyperlipidemia among men and women at different ages.

Method

Study Design and Population

This longitudinal cohort study was conducted to compare the rates of MetS in three age cohorts, born in 1956, 1960–1961, and 1964 in Yuci District, Jinzhong Prefecture, Shanxi Province, China. These age cohorts were chosen as part of a larger study comparing individuals born during (1960–1961 birth) with those born before and after (1954, 1956) the famine, respectively. Data were collected in the latter half of 2008 and 2012, respectively, in Yuci District (population 300,000). Yuci is a satellite city to the provincial capital of Taiyuan, and although many rural migrants have been absorbed into the city in recent years, in-migration from outside the province has been limited. Inclusion criteria required participants to have been born in Shanxi Province. Exclusion criteria included currently being treated for tuberculosis or cancer, taking corticosteroids, and pregnant.

Two thirds of the participants were recruited through 16 of 19 community health centers (CHC) in Yuci District, using the Health Record Database of each CHC, which contains the names of all enrolled individuals in its capitation area. Participants were recruited by phone invitation, posters in the community, and word of mouth. Intensity of recruitment varied by center, as did participation rate, with a high of 80% participation at one center but an average response rate of about 10%. Centers with a high population of residents born outside Jinzhong were not included in the data collection. The remaining one third of the participants were recruited through the Jinzhong First People's Hospital Health Examination Center. Individuals being examined at this facility are primarily healthy individuals whose employer arranges an annual physical exam. Informed consent was obtained from each participant before data collection.

A total of 806 people completed the cohort study in 2008, of which 13 were excluded because of failure to meet the inclusion criteria, resulting in a total of 793. A total of 638 completed the follow-up study in 2012, with a loss-to-follow-up rate of 19.5%. Of the 155 people who did not complete the follow-up study, 118 did not return, 16 refused, three died, six moved away, two developed serious disease, four were found to have been misclassified, five had incomplete records, and one was not fasting at the time of blood draw.

This research was done under the authority of the Shanxi Public Health Bureau and Yuci Public Health Bureau. It is the result of a collaboration between Shanxi Evergreen Service and the Jinzhong First People's Hospital, with the cooperation of Yuci Prefecture Women and Children's Hospital. The research proposal was approved by the Research Ethics Board (REB) of the University of Western Ontario and by the Jinzhong Prefecture Science Commission and Yuci District Public Health Bureau.

Data Collection

Laboratory. Overnight fasting blood samples were drawn by venipuncture to measure serum glucose, TG, total cholesterol, HDL, and low-density lipoproteins (LDL). All samples were analyzed within 3 hr at the Jinzhong People's Hospital Laboratory on a Roche Diagnostics Modular P800 Analyzer (Roche Diagnostics, Germany) using the reagent imported from Roche Diagnostics.

Anthropometric measurements. Body weight, height, and waist circumference were measured by trained staff according to the following protocol. Participants were weighed (without shoes) while wearing light summer clothes, and when the season changed, 1 to 2 kg were deducted to adjust for heavier fall and winter clothing. Standing height was measured in meters (without shoes) with the stadiometer attached to the scale (Su Hong Medical Equipment Company, Limited, Jiangsu, China). Measurements were taken to the nearest tenth of a centimeter. Waist circumference was measured with the participant standing erect using a standard tape measure. Measurement was taken at the umbilicus, the tape being horizontal and passing midway between the base of the rib cage and the iliac crest. BMI was calculated as kg/m^2.

Blood pressure measurement. At least two blood pressure measurements were obtained 1 min apart by trained nurses and physicians according to a standard protocol. The protocol was adapted from American Heart Association recommendations (Pickering et al., 2005). The blood pressure was the last procedure completed, to ensure that the participants had 30 min of rest after any exercise or smoking. A standard mercury sphygmomanometer was used, and this was calibrated at the Jinzhong People's Hospital Medical Equipment Department twice during the study. For this Chinese population, the standard cuff was suitable for all participants. All measurements were averaged.

Survey. A 47-item questionnaire was administered by trained research staff to all participants, assessing demographic data; personal medical history of hypertension, diabetes, and heart disease; physical activity of more than 150 min/week (moderate and vigorous activity done for more than 10 min a time, including commute, work, and leisure); smoking (never smoked, quit more than 1 year, and smoke at least one cigarette a day); and alcohol intake volume and frequency (never, occasional, quit, and twice a week or more). The physical activity–level items were taken from the Chinese version of the International Physical Activity Questionnaire (IPAQ; Liou, Jwo, Yao, Chiang, & Huang, 2008).

Definition of Metabolic Syndrome

The primary outcome measure was rate of MetS as defined by the revised NCEP ATP III criteria (Grundy, 2005). We used the Asian criteria for waist circumference (Heng et al., 2006). MetS is the presence of three or more of the following risk determinants:

1. increased waist circumference (≥ 90 cm for men, ≥ 80 cm for women);
2. elevated TG (TG ≥ 1.7 mmol/L [150 mg/dl]) or treatment for this lipid abnormality;
3. low high-density lipoprotein (HDL) cholesterol (HDL < 1.03 mmol/L [< 40 mg/dL] in men, HDL < 1.29 mmol/L [50 mg/dL] in women) or treatment for this lipid abnormality;
4. hypertension (≥ 130/≥ 85 mmHg) or treatment for hypertension; and
5. impaired fasting glucose (IFG ≥ 5.6 mmol/L [100 mg/dl]) or treatment for raised blood glucose.

Data Analysis

The first phase of the study (2008) included 793 participants. Phase 2 of the study (2012) included 643 of the original participants, for a follow-up rate of 81.08%. Responses from 643 participants who participated in both 2008 and 2012 were analyzed. Data on sociodemographic characteristics (gender, age, and employment status) and lifestyle (physical activity, alcohol intake, and smoking) were described using percentages, means, standard deviations, and 95% confidence intervals compared using ANOVA or chi-square tests. Odds ratios were calculated with logistic regression analysis, with all listed variables entered into the model simultaneously. Each disease was run separately. A 0.05 significance level was used for all tests. All analyses were performed using the statistical software SAS v 9.4 for Windows.

Results

In 2008, a higher proportion of men than women achieved 150 min/week of physical activity, although the difference was not statistically significant (Table 1). Four years later, 10% more women than men achieved the physical activity target, and the difference was significant. Nearly half of the men drank alcohol and around 62% of men smoked, and these proportions did not change from 2008 to 2012 (Table 1).

Table 1

Demographic Characteristics of the Study Sample

	Male sample (*n* = 210)		**Female sample (*n* = 428)**		***t* test *p* value**	
	n* (%) or *M* ± *SD		***n* (%) or *M* ± *SD***			
Characteristic	**2008**	**2012**	**2008**	**2012**	**2008**	**2012**
Age (years)	48.53 ± 3.08		48.44 ± 3.20		0.72	
Physical activity (> 150 min/week)	91 (43.33)	83 (39.52)	165 (38.55)	208 (48.60)	0.25	0.03

Table 1 (cont.)

Characteristic	Male sample (n = 210) n (%) or $M \pm SD$		Female sample (n = 428) n (%) or $M \pm SD$		t test p value	
	2008	**2012**	**2008**	**2012**	**2008**	**2012**
Alcohol	97 (46.19)	101 (48.10)	7 (1.64)	21 (4.91)	0.00	0.00
Smoking	129 (61.43)	131 (62.38)	5 (1.17)	4 (0.94)	0.00	0.00

Among the MetS components, men had higher blood pressure and higher fasting blood glucose at both time points, and these differences were statistically significant (Table 2). Men had higher mean TG levels and lower HDL levels than women did. Both TG and HDL levels remained the same for men from 2008 to 2012, but worsened for women (Table 2), contributing to increased rate of MetS among women (Table 3).

Table 2
Clinical Characteristics of the Study Sample

Characteristic	Male sample (n = 210) $M \pm SD$		Female sample (n = 428) $M \pm SD$		t test p value	
	2008	**2012**	**2008**	**2012**	**2008**	**2012**
Waist circumference (cm)	91.65 ± 8.7	90.00 ± 8.6	86.00 ± 8.9	84.37 ± 8.83	0.00	0.00
SBP (mm Hg)	128.60 ± 18.16	127.25 ± 16.46	123.24 ± 17.06	120.85 ± 15.67	0.00	0.00
DBP (mm Hg)	87.29 ± 11.91	85.68 ± 10.47	81.76 ± 10.60	79.74 ± 9.49	0.00	0.00
Blood Glucose (mmol/L)	6.03 ± 2.09	5.99 ± 1.88	5.51 ± 1.08	5.62 ± 1.32	0.00	0.01
Triglyceride	2.14 ± 1.84	2.01 ± 1.46	1.61 ± 1.06	1.77 ± 1.48	0.00	0.05
HDL (mmol/L)	1.15 ± 0.30	1.14 ± 0.30	1.39 ± 0.40	1.30 ± 0.33	0.00	0.00
LDL (mmol/L)	2.58 ± 0.95	2.68 ± 0.83	2.54 ± 0.79	2.79 ± 0.82	0.58	0.09

Table 3
Rate of Self-Reported Chronic Disease and Metabolic Syndrome

	Male sample (n = 210) $M \pm SD$		Female sample (n = 428) $M \pm SD$		Significance	
Characteristic	**2008**	**2012**	**2008**	**2012**	**2008**	**2012**
Hypertension	59 (28.10)	82 (39.05)	81 (18.93)	109 (25.47)	0.01	0.00
Diabetes	28 (13.33)	32 (15.24)	20 (4.67)	29 (6.78)	0.00	0.00
Hyperlipidemia	41 (19.52)	53 (25.24)	52 (12.15)	78 (18.22)	0.01	0.04
MetS	107 (50.95)	104 (49.52)	159 (37.15)	198 (46.26)	0.00	0.44

From 2008 to 2012, the self-reported rate of hypertension increased from 28.1% to 39.05% and from 18.9% to 25.5% for men and women, respectively (Table 3 and Figure 1). The same pattern of men with a higher rate than women, with both increasing from 2008 to 2012, was found with diabetes and hyperlipidemia. However, the rate of MetS in 2008 was 50.95% and 37.15% for men and women, respectively, but in 2012 the rate was 49.52% and 46.26% for men and women, respectively, a difference that was not statistically significant (p = 0.44; Table 3).

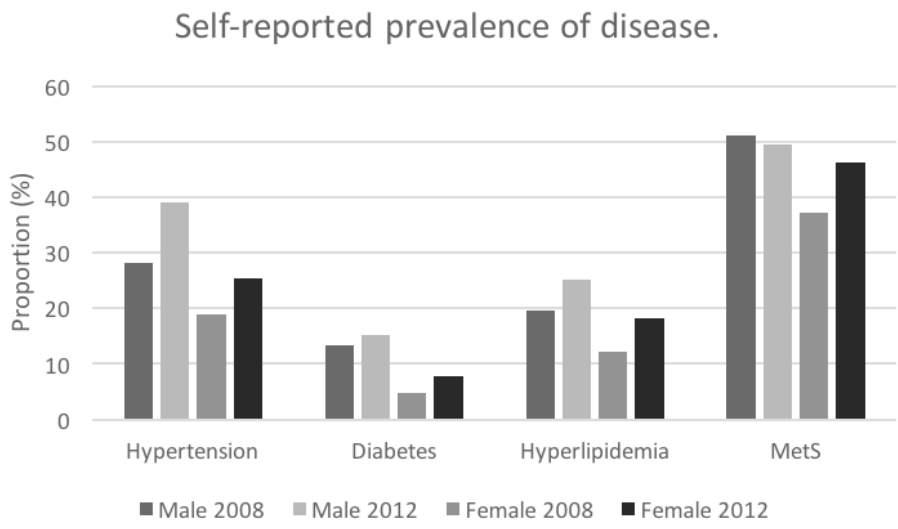

Figure 1. Self-reported prevalence of chronic disease by year and gender.

Logistic regression analysis was performed comparing predictor variables with each disease state. This analysis demonstrated that the presence of MetS in 2008 predicted the onset of incident hypertension, diabetes, and hyperlipidemia, with odds ratios of 2.51 (1.43, 4.41), 26.82 (3.46, 207.68), and 4.06 (2.41, 6.86), respectively (Table 4). Neither physical activity less than 150 min/week nor gender predicted onset of chronic diseases, and neither contributed to the regression model in a statistically significant manner (Table 4).

Table 4

Odds Ratio Estimate (95% CI) and Wald Confidence Intervals for Disease State as Dependent Variable (Controlled for Age, Gender, and Physical Activity Levels)

	Male sample (*n* = 210) *n* (%)		**Female sample (*n* = 428) *n* (%)**		**Significance**	
Characteristic	**2008**	**2012**	**2008**	**2012**	**2008**	**2012**
Hypertension	59 (28.10)	82 (39.05)	81 (18.93)	109 (25.47)	0.01	0.00
Diabetes	28 (13.33)	32 (15.24)	20 (4.67)	29 (6.78)	0.00	0.00
Hyperlipidemia	41 (19.52)	53 (25.24)	52 (12.15)	78 (18.22)	0.01	0.04
MetS	107 (50.95)	104 (49.52)	159 (37.15)	198 (46.26)	0.00	0.44

Discussion

In answer to the research question of this study, the presence of MetS in 2008 predicted the onset of incident hypertension, diabetes, and hyperlipidemia when we controlled for age. The prevalence of hypertension, diabetes, and hyperlipidemia were significantly higher among men than women at both time points, and the prevalence of all three increased from 2008 to 2012. The rate of MetS was significantly higher among men than among women in 2008, but the rate for women increased to be equivalent to that for men by 2012. In rural Shaanxi, S. Xu et al. (2014) found men to have higher rates of MetS from age 35–45 and women to surpass men at age 45 and beyond. Liang, Yan, Song, Cai, and Qiu (2013) showed that after age 60 the prevalence of MetS was 48.0% and 61.6% among men and women, respectively, which is in agreement with the results in the present study.

Neither physical activity less than 150 min/week nor gender predicted onset of chronic diseases, and neither contributed to the regression model in a statistically significant manner. The results of this study give confidence that the presence of MetS in a healthy middle-aged Chinese person can reasonably predict who will develop chronic diseases within the ensuing 4 years.

Men had higher blood pressure and higher fasting blood glucose than women did at both time points, and these differences were statistically significant. Men had higher mean TG and lower HDL levels than women did. Both TG and HDL levels remained the same for men, but worsened for women from 2008 to 2012. It has been shown among other Asian populations that postmenopausal women have increased LDL and TG levels (Furusyo et al., 2013). Therefore, weight control is of the utmost importance in preventing the cascade of events resulting in CVD and diabetes. A study of a rural Chinese population showed the peak mean TG level among men occurring at age 40–44, thereafter decreasing (Feng et al., 2006). In Jiangsu, China, Hu et al. (2006) found that the percentage of men with elevated TG peaked at 32% at age 35, declining thereafter, and the percentage of women with elevated TG rose steadily from 22% to 48% from age 40 to 65, when it plateaued.

It has been shown that insulin resistance (Reaven, 1988) and central adiposity (Carr et al., 2004) are the central underlying mechanisms through which MetS leads to CVD and diabetes. The MetS screening tool has been effectively used to predict impaired glucose tolerance; among those with MetS, the odds ratio for impaired glucose tolerance was 3–4, and the risk of developing diabetes was increased sixfold (Meigs et al., 2004). Among Chinese populations, blood glucose is the last MetS component to elevate. The Look AHEAD trial showed that once individuals have developed diabetes, intensive lifestyle interventions do not reduce their risk of myocardial infarction (Pi-Sunyer et al., 2007). Therefore, health promotion among Chinese populations should include diligent monitoring of blood glucose levels, with aggressive primary and secondary prevention to stop the progression to diabetes.

The observation that nearly half of men drank alcohol and around 62% of men smoked cigarettes and that these proportions did not change from 2008 to 2012 may be an indication of the underlying cause of these health outcomes among men. Men in China consume spirits more often than women do, contributing to MetS (Cai et al., 2012; Strand, Perry, & Wang, 2012). Smoking cessation appears to reduce the risk of MetS (Sun, Liu, & Ning, 2012). Key behavioral modification for health promotion activities in China should include management of alcohol intake, tobacco cessation, and increased physical activity (Strand et al., 2012; Strand, Perry, Wang, Liu, & Lynn, 2012). The effect of smoking on MetS was confounded by gender because the majority of men smoke and very few women smoke.

Although mortality due to CVD among women at age 45 is half that of men, it increases fourfold in women between ages 45 and 55 and is higher among menopausal women than men of comparable age (Kannel, Hjortland, McNamara, & Gordon, 1976; Prospective Studies Collaboration, 2002). Postmenopausal women in rural China had worse CVD risk factor profiles than did premenopausal women, which implied menopause might aggravate

the CVD epidemic beyond the effects of aging and would increase the CVD burden during and after their middle years (He et al., 2012).

Over the 4 years of this study, the proportion of men who achieved the physical activity target of 150 min/week did not change significantly, but the proportion of women who achieved the physical activity level target increased significantly and exceeded that of men by 2012. Many of the women in this study experienced menopause and the end of menses, which may have motivated them to exercise more to prevent weight gain. Some studies from non-Western countries have found menopause to predict MetS, but the results have been inconsistent (Carr, 2003; Estiaghi, Esteghamati, & Nakhjavani, 2010; Marroquin et al., 2004). It is also possible that many of the women in this study were retired by 2012, so they had more time to devote to exercise.

This study has contributed to the theoretical perspective that as China develops economically and socially, the people face increased risk of chronic disease onset. The ability of MetS to screen for individuals at increased risk of developing chronic diseases has also been shown, creating the opportunity for intervening in a way that compresses the duration of morbidity. Projections based on sample weighting suggest that China has 113.9 million people with diabetes and 493.4 million with prediabetes, so the economic and humanistic value of preventing diabetes in China cannot be overstated (Bragg et al., 2016; Y. Xu, Wang, & He, 2013). Clinical benefits of lifestyle intervention for patients with impaired glucose tolerance have been shown to effectively control the development of diabetes in Chinese populations (Li et al., 2014) Therefore, it is essential that preventive medicine do more to minimize weight gain and control blood glucose, blood pressure, and lipids earlier to prevent diabetes and CVD. By characterizing the differential onset of MetS by gender, this study contributes to the literature regarding the timing and content needed for men and women to prevent CVD and diabetes.

The people of Japan have the longest life expectancy in the world and arguably the most comprehensive national health care system. In 2008, the government of Japan implemented the National Metabolic Syndrome Examination and Health Guidance Mandate, which is a national screening program using MetS as a single point of entry to identify people who might benefit from an intervention to reduce CVD risk (Hosler, 2015; Kohro et al., 2008), and this has been followed up with interventions to test its effectiveness (Sakane et al., 2013). From 2008 to 2009, the prevalence of MetS declined by 21.2% and 29.7% among men and women after a year of intensive health guidance (Hosler, 2015). This demonstrates the ability to link lifestyle therapies, including weight reduction, increased physical activity, and an antiatherogenic diet, with scheduled MetS screening to reduce all of the components of MetS simultaneously (Rosenzweig et al., 2008). The only drugs that have the same effect are weight reduction drugs, but none of those are free of side effects. Therefore,

the presence of MetS is sufficient grounds to recommend the lifestyle modifications described above and thus offer prevention benefits for a cluster of diseases simultaneously.

Limitations

The generalizability of this study is limited to middle-aged people in urban areas of north central China. Disproportionate sampling by gender may have compromised the internal validity of this study, and small sample size compromised the statistical power of the study. Selection bias may have entered into the study as we do not know whether those lost to follow-up were different in any way. Dichotimizing the physiological parameters causes some loss of information, unless a threshold or bimodal distribution can be shown. However, MetS has been shown to be a consistent predictor of increased risk for CVD and diabetes (Kahn, Buse, Ferrannini, & Stern, 2005).

Future Research

The critical age when the rate of MetS among men increases could not be determined, because the rate of MetS for men in this study had already plateaued at the starting age of 44. This is a question that should be explored to better inform the timing of prevention efforts. The effect of menopause on CVD and diabetes also needs to be better understood. The third time point (2016) in this longitudinal study will determine whether rates for males and females continue the pattern observed here.

Future research should focus on clarifying the common metabolic pathways that underlie the development of diabetes and CVD, including those clustering within MetS. Population-based prevention strategies should also be developed and evaluated to determine context-specific reduction strategies that can be implemented in resource-limited settings (Simmons et al., 2010).

Conclusion

This longitudinal study has demonstrated the utility of the MetS screening tool to identify individuals at risk of developing hypertension, diabetes, or hyperlipidemia. The early onset and plateauing of MetS among men highlighted the importance of prevention efforts prior to the onset of risk factors among men, as early as in their 30s. In contrast, the delayed development of MetS among women and the steady increase with aging show that CVD and metabolic disorders are as important among women and require targeted prevention efforts unique to the needs of women. Elevated TG and elevated blood pressure were the most frequent risk factors for men, and elevated waist circumference and reduced HDL were the most frequent MetS risk factors among women. In an age when chronic diseases compromise the greatest contributor to burden of disease globally, MetS exists as a low-cost and highly feasible screening tool to use in early detection and prevention efforts.

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