total, el 56,0 % de los diabéticos no sabían que padecían la condición y solo el 39,5 % recibían tratamiento con frecuencia. La probabilidad de padecer diabetes en individuos de 55 a 59 años era casi el doble que en las mujeres de 35 a 39 años. Los participantes del estudio de los hogares más ricos tenían más posibilidades de padecer diabetes que aquellos de los más pobres. Además, la probabilidad de padecer diabetes también estuvo asociada de forma significativa con el nivel educativo, el peso corporal y la presencia de hipertensión. La prevalencia de diabetes varió según la región de residencia.

Conclusión Se halló que casi uno de cada diez adultos en Bangladesh padece diabetes, la cual se ha convertido recientemente en un problema de salud pública importante. Se necesitan medidas urgentes para contrarrestar el aumento de la diabetes, mediante la mejora de la detección, la conciencia, la prevención y el tratamiento.

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Table 1. **Characteristics of the study population aged 35 years or more, Bangladesh, 2011**

Characteristic	No. (%)[a,b]			P^c
	All (n = 7541)	No. without diabetes (n = 6746)	No. with diabetes (n = 795)	
Individual				
Age in years, mean ± SE	51.48 ± 0.17	51.31 ± 0.18	53.01 ± 0.54	< 0.01
Sex				0.19
Male	3721 (49.3)	3342 (49.6)	379 (46.9)	NA
Female	3820 (50.7)	3404 (50.4)	416 (53.1)	NA
Educational level				< 0.01
No education	3418 (48.2)	3156 (49.6)	262 (36.1)	NA
Primary education	2080 (26.8)	1869 (26.8)	211 (26.7)	NA
Secondary education	1403 (17.4)	1217 (16.9)	186 (21.3)	NA
Higher education	640 (7.6)	504 (6.7)	136 (15.9)	NA
Currently working				< 0.01
Yes	3898 (52.2)	3439 (51.5)	459 (58.7)	NA
No	3643 (47.8)	3307 (48.5)	336 (41.3)	NA
Marital status				0.09
Currently married	6329 (84.2)	5683 (84.5)	646 (81.8)	NA
Divorced, widowed or other	1212 (15.8)	1063 (15.5)	149 (18.2)	NA
Hypertension				< 0.01
Yes	5568 (74.5)	5093 (76.0)	475 (60.1)	NA
No	1973 (25.5)	1653 (24.0)	320 (39.9)	NA
Body weight				< 0.01
Normal	6915 (92.8)	6272 (93.9)	643 (82.8)	NA
Overweight or obese	626 (7.2)	474 (6.1)	152 (17.2)	NA
Household				
Socioeconomic status				< 0.01
Poorest	1343 (19.5)	1252 (20.3)	91 (12.7)	NA
Poorer	1351 (19.1)	1267 (19.8)	84 (12.2)	NA
Middle	1461 (19.8)	1364 (20.6)	97 (12.7)	NA
Richer	1581 (20.7)	1422 (20.6)	159 (21.8)	NA
Richest	1805 (20.9)	1441 (18.7)	364 (40.7)	NA
Community				
Place of residence				< 0.01
Urban	2480 (23.3)	2115 (22.0)	365 (35.4)	NA
Rural	5061 (76.7)	4631 (78.0)	430 (64.6)	NA
Region of residence				< 0.01
Khulna division	1204 (13.2)	1112 (13.7)	92 (8.6)	NA
Barisal division	860 (5.7)	755 (5.5)	105 (6.7)	NA
Chittagong division	1116 (16.7)	973 (16.1)	143 (21.4)	NA
Dhaka division	1312 (32.7)	1172 (32.5)	140 (33.4)	NA
Rajshahi division	1064 (14.4)	949 (14.3)	115 (14.4)	NA
Rangpur division	1068 (12.0)	977 (12.2)	91 (9.8)	NA
Sylhet division	917 (5.7)	808 (5.6)	109 (5.8)	NA

NA, not applicable; SE, standard error.

[a] All values represent absolute numbers and percentages unless otherwise stated.

[b] In estimating percentages, the complex survey design and sampling weights were taken into account.

[c] P-values were derived using a t test or χ^2 test for continuous and categorical variables, respectively.

Nationwide Survey of Prevalence and Risk Factors for Diabetes and Prediabetes in Bangladeshi Adults

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Diabetes is a major noncommunicable disease, ranking as a leading cause of death and disability worldwide (1). Globally, the prevalence of diabetes is ~8%, and nearly 80% of patients with diabetes live in low- and middle-income countries (2). Like many developing countries, prevalence of diabetes in Bangladesh increased substantially from 4% in 1990 to 10% in 2011 and is projected to reach 13% by 2030 (3,4). Despite this heavy burden, currently there are no epidemiologic studies in Bangladesh that investigate prevalence of diabetes and risk factors using nationally representative data. Therefore, we estimated the prevalence of diabetes and prediabetes and identified associated risk factors using Bangladesh nationwide survey data by multilevel logistic regression models.

Our analysis was based on the 2011 Bangladesh Demographic and Health Survey. Data were available as of February 2013, including 8,835 residents (4,524 men and 4,311 women) aged ≥35 years. The overall response rate was 89.17%. After dropping of nonresponders and missing data related to working status and hypertension, the remaining sample was 7,541. The estimated age-adjusted prevalence was taken into account for complex survey design and sampling weights.

Overall, 795 persons (9.7% [95% CI 4.2–10.5]) had diabetes, and 1,786 persons (23.0% [95% CI 21.3–24.7]) had prediabetes. Prevalence was nearly similar in both sexes (diabetes: men 9.3%, women 10.4%; prediabetes: men, 22.9%, women, 23.3%). Among diabetic persons, nearly 56.0% (95% CI 51.2–60.7) were unaware that they had diabetes. Only 39.5% (95% CI 35.1–44.1) of diabetic persons received treatment from consulting doctors regularly. In the multivariable logistic regression analyses, the odds of diabetes increased with increasing age (odds ratios of having diabetes for age-groups 35–39, 40–44, 45–49, 50–54,55–59, 60–69, and ≥70 years were 1.00 (reference), 1.17 [95% CI 0.86–1.57], 1.46 [1.09–1.96], 1.33 [0.97–1.82], 1.94 [1.40–2.68], 1.51 [1.09–2.08], and 1.82 [1.27–2.60], respectively) and with increasing weight (1.93 [1.52–2.47] among persons who were overweight/obese compared with normal-weight persons). The results also suggest that persons with higher education, those having hypertension, those belonging to the richest household, and the currently working group were more likely to have diabetes compared with their uneducated, nonhypertensive, poorest, and nonworking counterparts. Regarding prediabetes, age, education, and BMI showed a significant positive association. Bangladesh is a small country (147,570 km^2); however, there was a striking variation of being diabetic and prediabetic across the geographic regions. The highest age-adjusted prevalence of diabetes was observed in the southeastern part (Chittagong, 12.4%, and Barisal, 11.6%) of the country, followed by central (Dhaka, 10.2%), middle-western (Rajshahi, 10.2%), eastern (Sylhet, 10.0%), northwestern (Rajgpur, 8.0%), and western (Khulna, 6.4%) parts. Regression models revealed that residents in the southeastern part of Bangladesh were almost two times more likely to be diabetic compared with those living in western parts.

In conclusion, diabetes has become a major public health issue in Bangladesh, affecting one in ten adults. However, significant proportions of adults were unaware of their diabetes disease status, and few with diabetes received treatment regularly. These results suggest that urgent action is necessary to stop diabetes development through improving detection, awareness, prevention, and treatment of diabetes.

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Results Demographic and Health Surveys (MEASURE DHS) for providing permission to use the 2011 Bangladesh DHS data.

Duality of Interest. The authors obtained the data used in this study from the MEASURE DHS Archive. The data were originally collected by Macro International Inc. (Calverton, MD). No other potential conflicts of interest relevant to this article were reported.

Author Contributions. S.A. conceptualized the analysis plan for this study, drafted the manuscript, performed the statistical analysis, and reviewed and approved the final manuscript. M.M.R. conceptualized the analysis plan for this study, performed the statistical analysis, contributed to data interpretation and discussion, and reviewed and approved the final manuscript. S.K.A. contributed to data interpretation and discussion and reviewed and approved the final manuscript. P.S. critically revised the manuscript for important intellectual content and reviewed and approved the final manuscript. S.A. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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Table. Gallbladder Disease by Age Group for Both Women's Health Initiative Hormone Therapy Trials

	No. (%) of Participants With Gallbladder Disease		Hazard Ratio (95% CI)	P Value
	Hormone Therapy[a]	Placebo		
CEE alone trial				
All age groups	461 (1.64)	312 (1.06)	1.55 (1.34-1.79)	<.001
Age group, y				
50-59	157 (1.69)	117 (1.21)	1.40 (1.10-1.78)	
60-69	219 (1.78)	133 (1.01)	1.75 (1.41-2.17)	.66[b]
70-79	85 (1.32)	62 (0.93)	1.44 (1.04-2.00)	
CEE + MPA trial				
All age groups	528 (1.31)	319 (0.84)	1.57 (1.36-1.80)	<.001
Age group, y				
50-59	179 (1.24)	104 (0.77)	1.62 (1.27-2.06)	
60-69	254 (1.43)	152 (0.91)	1.57 (1.28-1.92)	.66[b]
70-79	95 (1.18)	63 (0.81)	1.47 (1.07-2.02)	

Abbreviations: CEE, conjugated equine estrogens; MPA, medroxyprogesterone acetate.

[a] Corresponds to CEE alone or CEE plus MPA.

[b] Indicates *P* value for interaction.

of gallbladder disease. For the CEE alone trial, the 2 HRs were 1.67 (95% CI, 1.35-2.06) and 1.55 (95% CI, 1.34-1.79), respectively.

To be able to compare directly the intervention and post-stopping findings, and due to the similarity of results using either of the above approaches, we chose to present the results for self-reported gallbladder disease in our recent article. This approach also allowed us to have approximately twice as many end points as were included in the earlier analysis because hospitalization records were not available for those who did not have overnight hospital stays or had outpatient procedures.

As shown in the Table, the tests for interaction by age group were not statistically significant in our analyses. Similar analyses of hospitalized cases used in the report by Cirillo et al[1] confirmed the absence of a statistically significant interaction by age (P = .13 for interaction with CEE + MPA and P = .08 for interaction with CEE alone). In these analyses, the HRs increased by age group in the CEE alone trial and decreased by age group in the CEE plus MPA trial, suggesting no consistent pattern by age.

We believe that the analyses of gallbladder disease presented in our recent report (and summarized in the Table) provide valid estimates for assessment of effect modification by age. Neither these analyses nor those based on the Cirillo et al[1] data set demonstrate consistent age trends.

Mounting evidence suggests that the transdermal route of estrogen administration, which avoids first-pass hepatic metabolism, may be less likely to increase the risk of gallbladder disease than the oral route of hormone delivery.[2]

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Prevention and Control of Hypertension in Different Countries

To the Editor Hypertension is the leading risk factor for death and disability worldwide. Dr Chow and colleagues[1] provided statistics on prevalence, awareness, treatment, and control of hypertension among selected high-, middle-, and low-income countries. The proportions of hypertension, awareness, treatment, and control reported in this article were strikingly different from other studies.[2-4]

For example, Chow et al[1] found that 39% of adults in Bangladesh had hypertension, whereas previous nationwide studies reported a prevalence of 25%.[3] The study also reported that about 40% of South Asian (Bangladesh, India, and Pakistan) adults were aware of their condition and 32% received treatment.

Previous studies from Bangladesh suggested about half of adults with hypertension were aware that they had it and 41% of the respondents with hypertension were receiving treatment,[3] which are comparatively higher than the figures of Chow et al.[1] Similar discrepancies also exist for India, China, and South Africa and may be due to a range of problems in the design and analysis of the study.

The data set of Chow et al[1] had small sample sizes and low response rates in low-income countries, in which typically response rates are high. The authors also did not strictly follow the probability sampling design or account for probability weights in their analysis. These shortcomings could have introduced selection bias and miscalculation of prevalence.

Chow et al[1] speculated that lower detection of hypertension may be due to costs and difficulties in accessing care. However, hypertension diagnosis in Bangladesh and many other low- and middle-income countries is almost free, and this minimal cost does not impose any financial burden on households.[4]

Low education, insufficient health facilities, and limited awareness of the need for testing could prevent diagnosis in rural or poor populations, and interventions to reduce these barriers to testing are more important than focusing on cost alone.

Accurate knowledge of prevalence, awareness, and treatment strategies helps policy makers to understand the present situation of hypertension and formulate appropriate national hypertension control policies. However, the results presented by Chow et al[1] may not help to improve understanding of this important disease.

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Conflict of Interest Disclosures: The authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and none were reported.

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In Reply Dr Rahman and Mr Gilmour raise concerns regarding the hypertension prevalence estimates in the Prospective Urban Rural Epidemiology (PURE) study, particularly for Bangladesh. We cautioned in the article that the sampling framework in each country was not nationally representative and therefore may not be representative of each country. The sample size in low-income countries was 31 685 and the response rate was 55%.

The analyses were not weighted because population census data were not available from all communities. Sampling was not identical across communities because of variation in the availability of population lists used for sampling. Hence, for practical reasons, investigators in each country, in consultation with the project office, identified the best method of sampling to obtain a representative sample of households in a community.

With respect to Bangladesh, there are important similarities and differences between the PURE study and the Bangladesh Demographic and Health Survey (BDHS).[1] Both studies were conducted by the same survey group. In the PURE study, the sample of 2754 was from households with participants aged 35 to 70 years. The BDHS (n = 7839) sampling framework excluded households with only older individuals, which may have led to a lower prevalence estimate due to selection bias.[1]

Importantly, the definitions used for hypertension differed. In the BDHS, the 25% prevalence[1] was based on people who had uncontrolled hypertension (≥140/90 mm Hg) or were taking an antihypertensive medication, but an additional 15% (oral communication, Shahidul Islam, Mitra and Associates, October 26, 2013) of people taking hypertension medication with controlled blood pressure were not classified as hypertensive. The PURE definition included both these groups. Therefore, the prevalence of controlled and uncontrolled hypertension in the BDHS of 40% is comparable with our value of 39%.

We did not report specifically on awareness, treatment, and control rates for Bangladesh in our article, but the differences in age and the definitions of hypertension used in the PURE study and the BDHS would have an effect on any comparison. Our figures for South Asia were 40.4% aware and 31.9% treated, and 40.8% aware and 31.7% treated in low-income countries (Table 2 in the article).

The reasons for lower detection and treatment of hypertension in low-income countries are likely to be multifactorial, as indicated in our article, including difficulties or costs in accessing health care, lack of knowledge about uncontrolled hypertension, and differing values. The interventions needed are therefore likely to be multifactorial as well.

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Patient-Reported Outcome Alert Monitoring

To the Editor In their Viewpoint on ethical and logistic considerations of using patient-reported outcome (PRO) measures in research, Mr Kyte and colleagues[1] discussed active PRO alert monitoring. In PRO alert monitoring, predefined thresholds for alert generation and action plans are established for when research participants report psychological or physical symptoms of potential concern.

Kyte et al[1] noted possible disadvantages of this approach, including that it may intrude upon participant privacy, it could lead to unwelcome offers of help, and knowledge of the approach could influence participant responses to PRO questionnaires.

However, Kyte et al[1] did not discuss another important problem: researchers would be in the position of conducting medical screening programs based on inadvertent positive scores on PRO questionnaires. Thus, researchers would be responsible for determining when screening across a potentially large number of conditions is ethical and justified based on evidence of potential benefits exceeding potential harms.

A concern is that this could lead to unwarranted and potentially harmful screening. Kyte et al[1] suggested psychological distress (eg, depression) as a sensible target for PRO alert monitoring. However, depression screening is only recommended in primary care settings by the US Preventive Services Task Force when integrated depression care systems are in place.[2] Few primary care settings and virtually no research groups meet this standard.

Depression screening is not recommended in Canada[3] or the United Kingdom,[4] and no well-conducted randomized clinical trials in any patient population have found that patients screened for depression have better depression outcomes than patients not screened.[3,4]

A Cochrane review[5] of 5 randomized clinical trials of depression screening in primary care found that none showed benefit, and the overall effect was virtually nil. Thus, it is reasonable to expect that participants in research settings would not benefit.

Screening always leads to costs and can result in unintended harms to some patients (eg, drug adverse effects, anxiety). The 2013 version of the Declaration of Helsinki (Article 17) specifies that all research involving human subjects must be preceded by a careful assessment of predictable risks and burdens, and that measures must be put into place to minimize risks.

If PRO alert monitoring is to be implemented, these same principles must be explicitly applied to potential benefits and harms that would be generated through this process. The PRO alerts should not be implemented unless there is reason to believe, based on evidence, that the benefits will exceed risks.

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In Reply Dr Thombs and colleagues make 2 overarching points. The first is that a system of active PRO alert monitoring is tantamount to screening, and second, that in the specific case of depression, screening is unlikely to be of benefit and may cause harm.

They conclude that, in line with the principles of the Declaration of Helsinki,[1] PRO alert monitoring should only be implemented when the potential benefits outweigh the potential harms and these potential harms are minimized. We agree with this conclusion. The purpose of our Viewpoint was to draw attention to this obligation in the context of PRO alerts and to open debate about how best to achieve this.

In our article, we described a number of methods currently in use for managing PRO alerts and suggested that a risk-based approach to management may be warranted. Thombs and colleagues cite a Cochrane review[2] stating that depression screening (in primary care) is of negligible benefit and should not be used in the research setting; however, within the review, a benefit that was not statistically significant was observed in a subgroup of trials including high-risk patients.

Accordingly, in trials enrolling patients at high risk of depression or suicide, monitoring responses may be both beneficial and minimize harm. It is less clear, however, whether this amounts to screening, inadvertent or otherwise.

The object is not to determine who "amongst those who are apparently well are suffering from disease."[3] Rather, the aim of PRO alert monitoring is to ensure that trial participants are as carefully observed with respect to PROs as they are for clinical outcomes.

Active PRO alert monitoring should not be implemented unless there is reason to believe (based on evidence) that the benefits will exceed the risks. The research community needs to establish whether an active monitoring approach for extreme PRO scores such as severe pain, depression, or suicidal thoughts is both beneficial and acceptable to patients, while determining the optimal thresholds used to trigger a response by the trial team.

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The Global Cardiovascular Risk Transition: Associations of Four Metabolic Risk Factors with National Income, Urbanization, and Western Diet in 1980 and 2008

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on behalf of the Global Burden of Metabolic Risk Factors of Chronic Diseases Collaborating Group

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The Global Cardiovascular Risk Transition

Associations of Four Metabolic Risk Factors with National Income, Urbanization, and Western Diet in 1980 and 2008

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Background**—**It is commonly assumed that cardiovascular disease risk factors are associated with affluence and Westernization. We investigated the associations of body mass index (BMI), fasting plasma glucose, systolic blood pressure, and serum total cholesterol with national income, Western diet, and, for BMI, urbanization in 1980 and 2008.

Methods and Results**—**Country-level risk factor estimates for 199 countries between 1980 and 2008 were from a previous systematic analysis of population-based data. We analyzed the associations between risk factors and per capita national income, a measure of Western diet, and, for BMI, the percentage of the population living in urban areas. In 1980, there was a positive association between national income and population mean BMI, systolic blood pressure, and total cholesterol. By 2008, the slope of the association between national income and systolic blood pressure became negative for women and zero for men. Total cholesterol was associated with national income and Western diet in both 1980 and 2008. In 1980, BMI rose with national income and then flattened at ≈Int$7000; by 2008, the relationship resembled an inverted U for women, peaking at middle-income levels. BMI had a positive relationship with the percentage of urban population in both 1980 and 2008. Fasting plasma glucose had weaker associations with these country macro characteristics, but it was positively associated with BMI.

Conclusions**—**The changing associations of metabolic risk factors with macroeconomic variables indicate that there will be a global pandemic of hyperglycemia and diabetes mellitus, together with high blood pressure in low-income countries, unless effective lifestyle and pharmacological interventions are implemented. (***Circulation*****. 2013;127:1493-1502.)**

Key Words: blood pressure ■ cholesterol ■ diabetes mellitus ■ epidemiology ■ obesity

Cardiovascular diseases (CVDs) are the leading cause of death and disease burden worldwide. Population aging leads to an increase in CVD deaths because CVD mortality rises with age. Beyond aging, age-specific mortality rates may increase or decline over time. Age-specific CVD death rates are themselves affected by exposure to risk factors such as excess weight; smoking; high blood pressure, cholesterol, and glucose; and by treatment availability and quality.

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Clinical Perspective on p 1502

Access to treatment tends to rise with income.[1] Although the association between CVD risk factors and socioeconomic status has been studied within countries,[1] few studies have assessed the cross-country association of CVD risk factors with national macroeconomic variables.[2–4] Some studies have postulated that CVD risk factors may rise with national income or urbanization, due to a Westernized diet and lifestyle,[5,6] referred to as diseases of affluence or Western diseases paradigm; others have concluded that higher income and urban infrastructure may help reduce CVD risk factors

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