SUPPLEMENTARY INFORMATION

(Appendix 1) Ethnicity distribution of the participants in the Kuwait National Health Registry

The data set contains information on a total of 270172 participants that visited the hospitals of the Ministry of Health. The participants include both natives and expatriates - Kuwaiti natives form 55%; Asian expatriates (largely from the Indian subcontinent) : 24%; Arab expatriates (largely from Egypt): 16%; and expatriates from other countries form 5%. Of the 270172 participants, 74134 are diagnosed with type 2 diabetes – ethnicity composition of the diabetes population is:- Kuwaiti natives: 51%; Asian expatriates: 29%; Arab expatriates: 15%; and expatriates from other continents: 5%. Of the 270172 participants, 58745 are diagnosed with hypertension – ethnicity composition of the hypertensive population is: Kuwaiti natives: 42% (=24672); Asian expatriates: 36%; Arab expatriates: 18%; and expatriates from other continents: 4%. Of the 270172 participants, 30522 are diagnosed with comorbidity of hypertension and type 2 diabetes– ethnicity composition of the comorbid population is: Kuwaiti natives: 57%; Asian expatriates: 25%; Arab expatriates: 14%; and expatriates from other continents: 4%.

(Appendix 2) Methods adopted in Kuwait primary health care centers to measure height, weight, HbA1c, and blood pressure

HbA1c measurements are made using the technique of high performance ion exchange liquid on glycohemoglobin analyzers. The Kuwait medical system utilizes the mercury type of sphygmomanometer to measure blood pressure. The participant is made to sit

quietly with the right arm placed on the table with the palm facing upwards. An appropriate cuff size is selected and wrapped securely with the lower edge 2 cm above the inner side of the elbow joint and kept at the same level of the heart. The brachial artery position is aligned. Disappearance of Korotkoff sound is used to register diastolic blood pressure. Average of three readings of blood pressure is recorded. Weight measurements are taken on a pre-calibrated electronic weighing scale that is placed on a firm flat surface. The participant is weighed dressed in light clothes, barefooted, facing forward and standing still. Weight is recorded to the nearest 100 grams. Height is measured to the nearest centimeter. Height is measured with the participant standing upright against a wall on which is fixed a height measuring device. The head is held in the Frankfort position and the heels are held together.

(Appendix 3) Diagnoses for diabetes and hypertension

Diagnoses for diabetes and hypertension are based on international guidelines and are performed mostly at the primary health care centers. Formal diagnostic criteria for type 2 diabetes are as below: a patient is declared type 2 diabetic if HbA1c (glycated hemoglobin) ≥ 6.5% OR FPG (fasting plasma glucose) ≥ 7.0 mmol/L OR 2hPG (2-hour plasma glucose in a 75g OGTT) ≥ 11.1 mmol/L OR random plasma glucose ≥ 11.1 mmol/L consistently in observations over a period of weeks to months. Though all the above four measurements are considered, a patient is declared diagnostic if symptoms are present with HbA1c or FPG.

Formal diagnostic criteria for hypertension are as below: a diabetic or non-diabetic patient is declared hypertensive if SBP (systolic blood pressure) >= 140 or DBP (diastolic blood pressure) >= 90 consistently in observations over a period of weeks to months. The JNC7 guidelines require that a diabetic patient with blood pressure readings of SBP = 120 to 139 OR DBP = 80 to 89 (pointing to prehypertension in general population) be diagnosed as hypertensive.

(Appendix 4) Methods used to carve out the CASE and CONTROL data sets

From the data set of 24672 native hypertensive patients, we carved out the following two data sets: (i) native comorbid patients with diagnosis of diabetes prior to that of hypertension (n=3904); and (ii) native hypertensive patients with no incidence of diabetes (n=1403).

The following sanity checks and filtering procedures were performed to shortlist the patients for consideration to carve out the above two data sets:-

(i) We considered only those participants who are not one-time or rare visitors to the clinics/hospitals, but are regular visitors before and after the diagnosis of diabetes and hypertension. We achieved this by laying a requirement that there exists at least 3 visits in the year prior to the diagnosis date; and that they have continued to visit the hospitals in the period leading to June 2012 (at which point we froze the data extraction for analysis in this study).

(ii) We considered only those participants for whom complete records of sex, onset age for hypertension, BMI (as recorded at the times of registration and of hypertension

onset) were available. We made sure that the recorded values for the different data items are consistent with one another and that measurements are not phenomenally outside the permitted ranges.

(iii) We further considered only those for whom the BMI measurements (along with others such as blood pressure readings) are available at regular intervals (of at least every 6 months) over the period from registration to onset of hypertension.

(iv) It is necessary is to make sure that the patients have been regularly monitored for onset of diabetes and hypertension – this ensures that the date of diagnosis is as close as possible to the date of onset. This is achieved by the checks mentioned in the above three steps of (I to iii).

(v) We ascertained that the diabetic patients diagnosed with hypertension have blood pressure readings of (SBP ≥ 140 OR DBP ≥90) consistently in the period around diagnosis of hypertension. Though JNC 7 guidelines (released in 2003) recommends lower threshold values for blood pressure in diabetic patients, the above-mentioned higher threshold values were used since the participants from the final list of 6204 are seen to have their hypertension diagnosed during the years 2000 to 2012.

(vi) The above requirements were seen satisfied in the case of only 6204 out of 24672 participants. We further made sure that the date of diagnosis of hypertension refers to actual date of onset by using the following checks: whether any of the 6204 patients had been prescribed anti-hypertensive medication or had abnormal blood pressure readings during the period preceding the diagnosis for hypertension.

These sanity checks brought down the number of patients to 5882, from which the two data sets of cases and controls are carved.

(Appendix 5) Testing the associations between BMI and age at onset of hypertension for confounding due to anti-diabetic medication

We observe that 28.4% of the participants that form the data set of hypertension in diabetic patients are seen to be administered anti-diabetic medication in the year preceding the onset of hypertension. We evaluate whether anti-diabetic medication impacts the BMI associations with hypertension by considering anti-diabetic medication status as an additional covariate to build a revised regression model for the data set of hypertension in diabetic patients. We find that the coefficient of medication status term is statistically insignificant (p-value= 0.4), and that the slope for the association of BMI with age at onset of hypertension remains the same, at -0.39; Thus the anti-diabetic medication status does not seem to confound the derived associations.