

Supplementary Material:

SITE LOCATIONS FOR TANDEM STUDY

Summary - Study site locations

In Bandung, Indonesia, diabetes mellitus (DM) patients were recruited in 25 community health centres and from the Endocrine clinic in a tertiary public referral hospital. In Lima, Peru, patients were recruited at recruited at diabetes clinic at one tertiary level public hospital in Lima. In Romania, patients with DM were recruited from two secondary level hospitals in Craiova. In South Africa, patients were recruited at three community health care clinics in the northern Cape Town metropolitan area.

Country and site selection

For the TANDEM study, it was important to select countries from different geographic regions so that diverse cultural, health system structures and population demographics could be represented. The burden of TB and DM also needed to be sufficiently high so that there would be sufficient TB-DM burden within the populations to be able to detect a causal effect. The countries also needed to be typical of settings where economic improvement and changes in lifestyles would be likely to increase the risk of DM substantially. During the TANDEM proposal development in 2011, current data indicated that Peru and Romania had some of the highest TB incidence rates in the South American and European regions respectively (106 and 159 per 100,000 population respectively) and an expected increase of DM between 90% and 160% (WHO, 2010a). With a TB incidence of 189 per 100,000 population (WHO, 2010a), Indonesia's burden was well above the recommended screening threshold for TB in people with DM of 100 per 100,000, as recommended by the WHO/Union Framework

(The Union and WHO, 2011), even though it was not one of the highest in the South-East Asia region at that time.

The feasibility of conducting the studies was also an important criterion in the country selection and this was largely informed by long-term pre-existing research relationships between the TANDEM project principal investigators and research institutions within the countries as well as the collaborators' capacity to recruit, test and treat patients for TB and DM and their access to potential participants. Given these considerations, Indonesia, Peru, Romania, and South Africa each with a high burden of TB and an increasing prevalence of DM, were selected.

The Universitas Padjadjaran (UNPAD) Teaching Hospital research team in west Bandung, Indonesia has a pre-existing research relationship with Hasan Sadikin Hospital (RSHS), thus the Endocrine clinic at RSHS was selected for recruitment of people with DM. The Community Health Centres (Puskesmas') with a large number of patients with DM in Bandung were contacted and asked to participate in the TANDEM study, with the permission and endorsement of the City Health Office. Additional patients with DM were recruited from those facilities.

In Peru, TANDEM made a request to the Ministry of Health to get permission and access to health facilities in Lima to conduct the study. The Ministry of Health then provided a list of facilities with sufficient patient volume to meet the Peru recruitment targets and that were not already involved in another research project, conducted by any other local or international institution. HAMA, the reference hospital for almost one million people in South Lima, was chosen for recruitment of people with DM since the

Endocrine Department and the daily DM clinic are the most accessed DM services in the area, particularly by uninsured people with DM.

In Romania, sites were also purposively selected based on pre-existing research collaborations with the country principal investigator in Dolj and Gorj counties as well as a high volume of DM patients at the two general hospitals Victor Babes Hospital and the Runcu Hospital.

In South Africa, all clinical sites used for recruitment were located in the northern part of the Cape Town metropolitan area. The facilities were selected because they are relatively close to Stellenbosch University's Faculty of Medicine and Health Sciences and cater for people with low- to lower-middle income for whom interventions are most needed. The areas have previously been reported to have a high prevalence of TB and diabetes, and the study team have a longstanding relationship with the personnel due to previous research activities. DM patients were recruited from three Community Health Centres, under the management of Western Cape Provincial Health Department.

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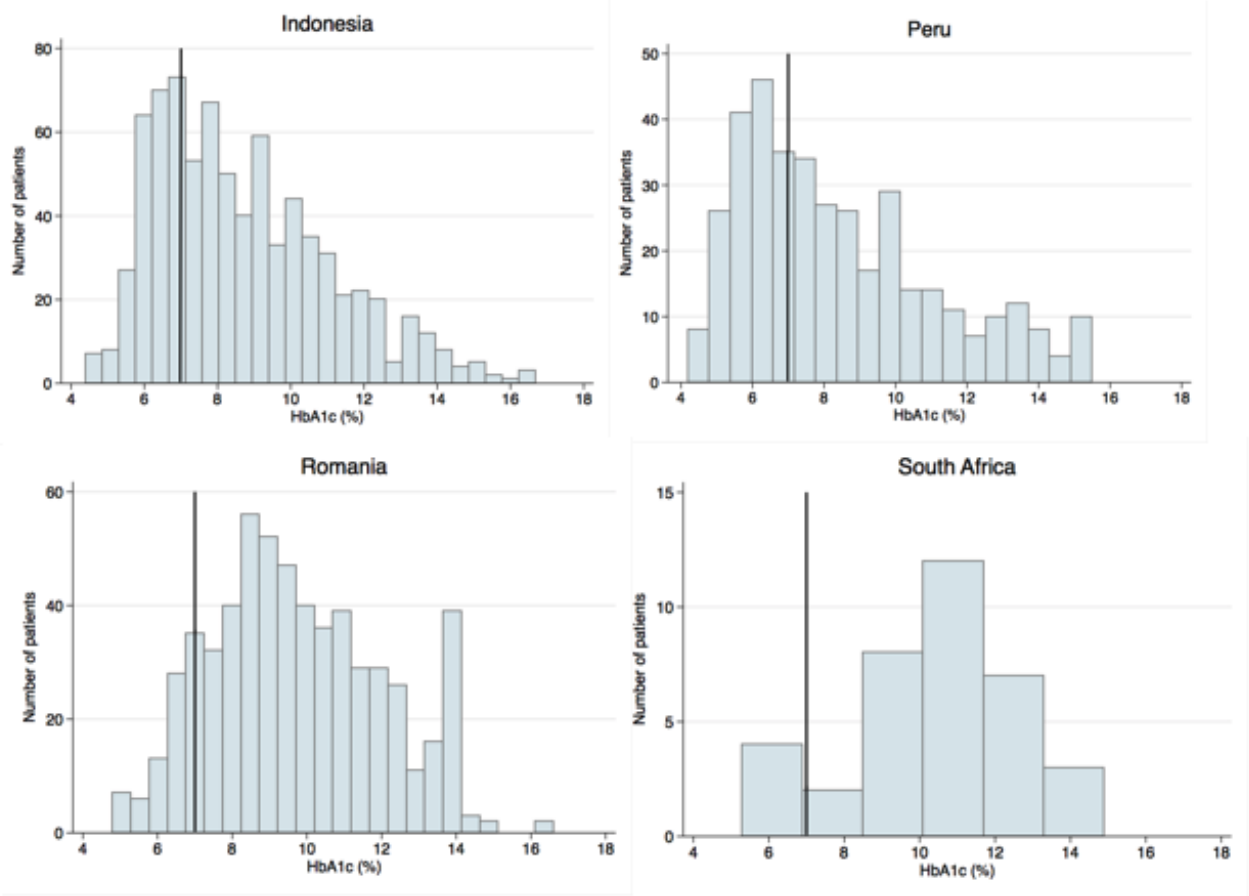


Figure 1. Distribution of HbA1c values for each recruitment site

The proportion of patients reaching the treatment target of HbA1c < 7% (53 mmol/mol) (vertical black line) was 28.2% for Indonesia (n=780), 38.0% for Peru (n=379), 11.1% for Romania (n=588), and 11.1% for South Africa (n=36).

Table S.1. Indonesia (n=783): Univariate and multivariate analyses of risk factors for inadequately controlled diabetes (HbA1c \geq 10 (86 mmol/mol)), macrovascular and microvascular complications

		HbA1c \geq 10 (86 mmol/mol)		Macrovascular complications		Microvascular complications	
		Univariate Odds ratio (95% CI)	Multivariate* Odds ratio (95% CI)	Univariate Odds ratio (95% CI)	Multivariate* Odds ratio (95% CI)	Univariate Odds ratio (95% CI)	Multivariate* Odds ratio (95% CI)
Sex:	Female vs. male	0.87 (0.63-1.21)	1.14 (0.80-1.64)	2.01 (1.41-2.85)	1.81 (1.24-2.63)	0.74 (0.54-1.00)	0.72 (0.51-1.00)
Age:	<59	1.0	1.0	1.0	1.0	1.0	1.0
	59+	0.46 (0.33-0.63)	0.45 (0.32-0.64)	1.68 (1.18-2.38)	1.50 (1.02-2.20)	1.47 (1.10-1.98)	1.29 (0.83-2.00)
Education:	Less than primary completed	1.0	1.0	1.0	1.0	1.0	1.0
	Secondary completed	0.96 (0.62-1.49)	1.00 (0.63-1.59)	1.34 (0.79-2.28)	1.35 (0.78-2.33)	1.31 (0.86-2.01)	1.29 (0.83-2.00)
	High school completed	0.68 (0.46-1.02)	0.75 (0.48-1.18)	1.59 (0.99-2.53)	1.40 (0.84-2.33)	1.06 (0.72-1.56)	1.08 (0.71-1.66)
	College/university/post graduate	0.53 (0.34-0.83)	0.64 (0.37-1.09)	1.57 (0.96-2.58)	1.23 (0.69-2.20)	0.98 (0.65-1.48)	0.91 (0.56-1.48)
Socio-economic status**	Q1-Q2	1.0	1.0	1.0	1.0	1.0	1.0
	Q3	0.81 (0.50-1.29)	0.83 (0.50-1.35)	1.75 (1.01-3.03)	1.60 (0.91-2.82)	0.98 (0.61-1.56)	1.02 (0.63-1.65)
	Q4-Q4	0.56 (0.39-0.80)	0.72 (0.48-1.09)	1.38 (0.90-2.13)	0.99 (0.60-1.62)	1.02 (0.75-1.44)	0.96 (0.64-1.42)
DM duration	<1 year	1.0	1.0	1.0	1.0	1.0	1.0
	1-5 years	0.92 (0.59-1.43)	0.99 (0.62-1.57)	0.95 (0.57-1.59)	0.95 (0.56-1.60)	1.40 (0.89-2.20)	1.36 (0.85-2.16)
	6-15 years	0.96 (0.61-1.50)	1.25 (0.77-2.01)	1.02 (0.62-1.72)	0.98 (0.57-1.68)	1.84 (1.17-2.90)	1.75 (1.09-2.81)
	>15 years	0.69 (0.30-0.62)	1.19 (0.58-2.47)	2.15 (1.11-4.14)	1.78 (0.87-3.57)	4.09 (2.20-7.61)	3.72 (1.94-7.13)

* All variables (sex, age, education, socio-economic status & DM duration) are included in the model

** Socio-economic status: Q1: poorest; Q2: poor; Q3: middle income; Q4: upper middle income; Q5: richest

Table S.2. Peru (n=599): Univariate and multivariate analyses of risk factors for inadequately controlled diabetes (HbA1c ≥ 10 (86 mmol/mol)), macrovascular and microvascular complications

		HbA1c ≥ 10 (86 mmol/mol) [‡]		Macrovascular complications		Microvascular complications	
		Univariate Odds ratio (95% CI)	Multivariate* Odds ratio (95% CI)	Univariate Odds ratio (95% CI)	Multivariate* Odds ratio (95% CI)	Univariate Odds ratio (95% CI)	Multivariate* Odds ratio (95% CI)
Sex:	Female vs. male	1.18 (0.71-1.95)	1.14 (0.64-2.01)	1.30 (0.72-2.32)	1.10 (0.59-2.06)	0.68 (0.45-1.02)	0.83 (0.53-1.30)
Age:	<59	1.0	1.0	1.0	1.0	1.0	1.0
	59+	0.69 (0.43-1.10)	0.61 (0.35-1.06)	1.54 (0.87-2.74)	1.41 (0.74-2.69)	1.61 (1.09-2.37)	1.11 (0.71-1.73)
Education:	Less than primary completed	1.0	1.0	1.0	1.0	1.0	1.0
	Secondary completed	1.03 (0.55-1.92)	0.87 (0.44-1.71)	1.28 (0.62-2.64)	1.43 (0.66-3.08)	0.50 (0.30-0.84)	0.56 (0.32-0.98)
	High school completed	1.69 (0.99-2.88)	1.40 (0.78-2.52)	1.16 (0.60-2.23)	1.27 (0.62-2.60)	0.40 (0.26-0.63)	0.44 (0.27-0.73)
	College/university/post graduate	1.12 (0.29-4.33)	0.86 (0.20-3.73)	1.26 (0.28-5.75)	1.47 (0.29-7.38)	0.25 (0.09-0.66)	0.31 (0.11-0.85)
Socio-economic status**	Q1-Q2	1.0	1.0	1.0	1.0	1.0	1.0
	Q3	1.03 (0.52-2.02)	1.10 (0.55-2.19)	0.48 (0.20-1.17)	0.51 (0.21-1.24)	0.68 (0.40-1.15)	0.69 (0.40-1.21)
	Q4-Q5	1.51 (0.90-2.55)	1.39 (0.80-2.41)	0.92 (0.51-1.66)	0.94 (0.51-1.75)	0.71 (0.45-1.11)	0.90 (0.56-1.45)
DM duration	<1 year	1.0	1.0	1.0 [§]	1.0	1.0	1.0
	1-5 years	0.76 (0.40-1.44)	0.87 (0.45-1.68)	1.57 (0.64-3.81)	1.58 (0.64-3.89)	1.74 (1.07-2.83)	1.63 (0.98-2.71)
	6-15 years	1.54 (0.81-2.93)	1.89 (0.97-3.71)	2.37 (0.95-5.92)	2.17 (0.85-5.53)	1.69 (0.97-2.93)	1.51 (0.85-2.69)
	>15 years	1.35 (0.64-2.83)	1.84 (0.81-4.20)	2.42 (0.92-6.43)	2.14 (0.77-5.97)	2.32 (1.21-4.48)	2.07 (1.02-4.18)

*All variables (sex, age, education, socio-economic status & DM duration) are included in the model

** Socio-economic status: Q1: poorest; Q2: poor; Q3: middle income; Q4: upper middle income; Q5: richest

[‡] HbA1c available for 379 participants

[§] Test for trend significant at $p < 0.05$

Table S.3. Romania (n=603): Univariate and multivariate analyses of risk factors for inadequately controlled diabetes (HbA1c ≥ 10 (86 mmol/mol)), macrovascular and microvascular complications

		HbA1c ≥ 10 (86 mmol/mol) [‡]		Macrovascular complications		Microvascular complications	
		Univariate Odds ratio (95% CI)	Multivariate* Odds ratio (95% CI)	Univariate Odds ratio (95% CI)	Multivariate* Odds ratio (95% CI)	Univariate Odds ratio (95% CI)	Multivariate* Odds ratio (95% CI)
Sex:	Female vs. male	0.76 (0.55-1.05)	0.89 (0.62-1.27)	1.01 (0.70-1.47)	1.11 (0.74-1.66)	0.63 (0.46-0.87)	0.74 (0.52-1.06)
Age:	<59	1.0	1.0	1.0	1.0	1.0	1.0
	59+	0.85 (0.62-1.19)	0.83 (0.57-1.21)	2.46 (1.67-3.62)	2.52 (1.65-3.87)	1.74 (1.26-2.41)	1.27 (0.88-1.83)
Education:	Less than primary completed	1.0	1.0	1.0	1.0	1.0	1.0
	Secondary completed	0.50 (0.29-0.85)	0.59 (0.33-1.06)	0.97 (0.55-1.72)	0.91 (0.48-1.72)	0.70 (0.40-1.22)	0.69 (0.38-1.27)
	High school completed	0.39 (0.23-0.65)	0.43 (0.24-0.79)	0.81 (0.46-1.42)	0.92 (0.47-1.76)	0.38 (0.22-0.65)	0.43 (0.23-0.80)
	College/university/post graduate	0.30 (0.15-0.61)	0.37 (0.17-0.83)	0.65 (0.29-1.43)	0.57 (0.23-1.40)	0.32 (0.16-0.64)	0.31 (0.14-0.68)
Socio-economic status**	Q1-Q2	1.0	1.0	1.0	1.0	1.0	1.0
	Q3	0.46 (0.28-0.77)	0.56 (0.33-0.97)	1.24 (0.70-2.21)	1.18 (0.63-2.19)	0.72 (0.44-1.19)	0.75 (0.43-1.29)
	Q4-Q5	0.50 (0.33-0.75)	0.71 (0.45-1.14)	1.22 (0.76-1.97)	1.43 (0.83-2.47)	0.79 (0.52-1.18)	0.93 (0.57-1.49)
DM duration	<1 year	1.0	1.0	1.0	1.0	1.0	1.0
	1-5 years	0.39 (0.22-0.66)	0.40 (0.23-0.70)	2.59 (1.25-5.35)	2.72 (1.29-5.77)	1.54 (0.92-2.59)	1.89 (1.09-3.27)
	6-15 years	0.29 (0.19-0.46)	0.32 (0.20-0.52)	3.02 (1.59-5.73)	2.59 (1.35-4.99)	1.92 (1.23-2.98)	2.11 (1.33-3.37)
	>15 years	0.23 (0.14-0.40)	0.26 (0.15-0.45)	5.03 (2.53-9.97)	4.23 (2.09-8.55)	6.17 (3.47-10.97)	7.06 (3.81-13.07)

* All variables (sex, age, education, socio-economic status & DM duration) are included in the model

** Socio-economic status: Q1: poorest; Q2: poor; Q3: middle income; Q4: upper middle income; Q5: richest

[‡] HbA1c available for 588 participants

Table S.4. Indonesia: Univariate and multivariate analyses of factors associated with medical management for patients indicated for treatment (patients with HbA1c ≥ 10 (86 mmol/mol) receiving insulin, patients with hypertension taking anti-hypertensives, patients with cardiovascular complications taking aspirin)

		Patients with HbA1c ≥ 10 (86 mmol/mol) (n=221) receiving insulin		Patients with hypertension (n=439) taking anti-hypertensives		Patients with cardiovascular (n=140) complications taking aspirin	
		Univariate Odds ratio (95% CI)	Multivariate* Odds ratio (95% CI)	Univariate Odds ratio (95% CI)	Multivariate* Odds ratio (95% CI)	Univariate Odds ratio (95% CI)	Multivariate* Odds ratio (95% CI)
Sex:	Female vs. male	2.11 (1.17-3.80)	2.26 (1.16-4.42)	0.50 (0.32-0.78)	0.43 (0.26-0.70)	1.33 (0.58-3.07)	0.76 (0.28-2.05)
Age:	<59	1.0	1.0	1.0	1.0	1.0	1.0
	59+	0.69 (0.38-1.27)	0.56 (0.28-1.11)	1.76 (1.16-2.66)	2.29 (1.44-3.62)	1.68 (0.68-4.14)	1.51 (0.51-4.47)
Education:	Less than primary completed	1.0	1.0	1.0	1.0	1.0	1.0
	Secondary completed	1.63 (0.74-3.60)	1.57 (0.67-3.63)	0.94 (0.53-1.65)	0.96 (0.53-1.77)	4.57 (0.84-24.8)	4.27 (0.71-25.52)
	High school completed	2.23 (1.07-4.65)	1.71 (0.74-3.95)	0.65 (0.38-1.11)	0.77 (0.42-1.42)	4.36 (0.87-21.8)	2.98 (0.53-16.76)
	College/university/post graduate	1.33 (0.56-3.20)	1.03 (0.36-2.89)	0.93 (0.54-1.61)	1.13 (0.58-2.20)	6.77 (1.37-33.3)	3.94 (0.59-26.49)
Socio-economic status**	Q1-Q2	1.0	1.0	1.0	1.0	1.0	1.0
	Q3	0.67 (0.28-1.60)	0.56 (0.22-1.40)	0.86 (0.45-1.65)	0.90 (0.46-1.77)	1.64 (0.25-10.73)	1.99 (0.28-14.24)
	Q4-Q5	1.22 (0.51-2.94)	0.72 (0.34-1.52)	0.82 (0.51-1.32)	0.93 (0.53-1.63)	4.00 (0.87-18.31)	3.19 (0.59-17.32)
DM duration	<1 year	1.0	1.0	1.0	1.0	1.0	1.0
	1-5 years	2.06 (0.84-5.05)	2.26 (0.89-5.72)	1.17 (0.64-2.12)	0.95 (0.51-1.78)	0.51 (0.16-1.66)	0.35 (0.09-1.31)
	6-15 years	2.30 (0.94-5.63)	2.70 (1.05-6.96)	0.76 (0.41-1.38)	0.55 (0.29-1.06)	0.60 (0.19-1.89)	0.35 (0.09-1.28)
	>15 years	2.06 (0.55-7.74)	3.07 (0.72-13.07)	1.12 (0.51-2.48)	0.72 (0.31-1.71)	1.14 (0.32-4.10)	0.61 (0.14-2.60)

* All variables (sex, age, education, socio-economic status & DM duration) are included in the model

** Socio-economic status: Q1: poorest; Q2: poor; Q3: middle income; Q4: upper middle income; Q5: richest

Table S.5. Peru: Univariate and multivariate analyses of factors associated with medical management for patients indicated for treatment (patients with HbA1c ≥ 10 (86 mmol/mol) receiving insulin, patients with hypertension taking anti-hypertensives, patients with cardiovascular complications taking aspirin)

		Patients with HbA1c ≥ 10 (86 mmol/mol) (n=98) receiving insulin		Patients with hypertension(n=129) taking anti-hypertensives		Patients with cardiovascular complications (n=46) taking aspirin	
		Univariate Odds ratio (95% CI)	Multivariate* Odds ratio (95% CI)	Univariate Odds ratio (95% CI)	Multivariate* Odds ratio (95% CI)	Univariate Odds ratio (95% CI)	Multivariate* Odds ratio (95% CI)
Sex:	Female vs. male	0.55 (0.22-1.38)	0.65 (0.21-2.03)	1.85 (0.87-3.96)	1.70 (0.68-4.23)	1.28 (0.36-4.52)	0.94 (0.71-5.34)
Age:	<59	1.0	1.0	1.0	1.0	1.0	1.0
	59+	1.57 (0.69-3.52)	0.99 (0.36-2.74)	1.90 (0.88-4.10)	1.69 (0.69-4.13)	1.18 (0.33-4.17)	1.07 (0.16-7.20)
Education:	Less than primary completed	1.0	1.0	1.0	1.0	1.0	1.0
	Secondary completed	0.40 (0.11-1.41)	0.62 (0.15-2.63)	1.28 (0.49-3.35)	1.18 (0.39-3.55)	8.00 (1.31-48.6)	6.42 (0.68-60.3)
	High school completed	1.39 (0.56-3.43)	3.59 (1.07-12.09)	0.75 (0.29-1.92)	0.61 (0.20-1.87)	3.20 (0.75-13.7)	4.14 (0.73-23.42)
	College/university/post graduate	0.69 (0.06-3.43)	1.83 (0.10-32.02)	0.77 (0.12-4.89)	1.94 (0.22-16.75)	-	-
Socio-economic status**	Q1-Q2	1.0	1.0	1.0	1.0	1.0	1.0
	Q3	1.89 (0.56-6.24)	2.01 (0.51-7.95)	0.45 (0.19-1.10)	0.44 (0.17-1.14)	2.25 (0.32-15.76)	3.27 (0.33-32.28)
	Q4-Q5	0.65 (0.26-1.65)	0.48 (0.16-1.47)	0.43 (0.19-0.99)	0.40 (0.16-1.01)	0.72 (0.20-2.57)	0.80 (0.15-4.14)
DM duration	<1 year	1.0 [§]	1.0	1.0	1.0	1.0 [§]	1.0 [§]
	1-5 years	0.75 (0.21-2.60)	0.87 (0.22-3.44)	3.96 (1.02-15.37)	4.02 (0.96-16.84)	1.33 (0.11-15.70)	0.60 (0.04-9.49)
	6-15 years	2.14 (0.69-6.66)	3.42 (0.89-13.14)	5.88 (1.45-23.80)	5.73 (1.30-25.13)	5.33 (0.47-60.80)	3.35 (0.19-60.49)
	>15 years	3.06 (0.82-11.44)	3.67 (0.77-17.55)	7.22 (1.60-32.10)	7.02 (1.39-35.31)	10.67 (0.82-138.22)	5.85 (0.35-97.36)

* All variables (sex, age, education, socio-economic status & DM duration) are included in the model

** Socio-economic status: Q1: poorest; Q2: poor; Q3: middle income; Q4: upper middle income; Q5: richest

§ Test for trend significant at $p < 0.05$

Table S.6. Romania: Univariate and multivariate analyses of factors associated with medical management for patients indicated for treatment (patients with HbA1c ≥ 10 (86 mmol/mol) receiving insulin, patients with hypertension taking anti-hypertensives, patients with cardiovascular complications taking aspirin)

		Patients with HbA1c ≥ 10 (86 mmol/mol) (n=252) receiving insulin		Patients with hypertension(n=295) taking anti-hypertensives		Patients with cardiovascular complications (n=133) taking aspirin	
		Univariate Odds ratio (95% CI)	Multivariate* Odds ratio (95% CI)	Univariate Odds ratio (95% CI)	Multivariate* Odds ratio (95% CI)	Univariate Odds ratio (95% CI)	Multivariate* Odds ratio (95% CI)
Sex:	Female vs. male	1.07 (0.58-1.98)	1.32 (0.66-2.67)	0.72 (0.44-1.17)	0.86 (0.50-1.47)	1.64 (0.79-3.42)	1.74 (0.73-4.16)
Age:	<59	1.0	1.0	1.0	1.0	1.0	1.0
	59+	1.25 (0.68-2.31)	0.89 (0.44-1.83)	1.84 (1.12-3.02)	1.55 (0.90-2.67)	0.46 (0.21-0.98)	0.34 (0.13-0.86)
Education:	Less than primary completed	1.0	1.0	1.0	1.0	1.0	1.0
	Secondary completed	0.91 (0.34-2.47)	0.58 (0.19-1.81)	0.92 (0.41-2.08)	0.96 (0.40-2.31)	1.65 (0.47-5.83)	0.85 (0.20-3.53)
	High school completed	0.39 (0.15-0.96)	0.29 (0.10-0.89)	0.32 (0.15-0.69)	0.35 (0.15-0.82)	2.15 (0.63-7.45)	0.92 (0.23-3.75)
	College/university/post graduate	0.61 (0.16-2.38)	0.53 (0.11-2.47)	1.10 (0.36-3.40)	1.11 (0.32-3.78)	2.14 (0.41-11.17)	0.67 (0.10-4.59)
Socio-economic status**	Q1-Q2	1.0	1.0	1.0	1.0	1.0 [§]	1.0
	Q3	0.73 (0.30-1.77)	0.79 (0.29-2.19)	0.88 (0.43-1.77)	0.89 (0.42-1.92)	2.76 (0.74-10.29)	2.54 (0.60-10.80)
	Q4-Q5	1.00 (0.49-2.03)	1.23 (0.52-2.94)	1.06 (0.59-1.93)	1.29 (0.65-2.55)	3.10 (0.97-9.95)	2.24 (0.62-8.10)
DM duration	<1 year	1.0	1.0	1.0	1.0	1.0	1.0
	1-5 years	1.85 (0.80-4.28)	1.60 (0.66-3.97)	0.58 (0.26-1.29)	0.83 (0.35-1.95)	0.56 (0.10-3.10)	0.26 (0.04-1.84)
	6-15 years	2.60 (1.27-5.35)	2.35 (1.09-5.03)	0.83 (0.52-1.65)	0.79 (0.38-1.66)	1.67 (0.40-7.00)	1.86 (0.40-8.71)
	>15 years	-	-	1.46 (0.62-3.43)	1.36 (0.55-3.35)	1.38 (0.32-6.05)	1.69 (0.34-8.34)

* All variables (sex, age, education, socio-economic status & DM duration) are included in the model

** Socio-economic status: Q1: poorest; Q2: poor; Q3: middle income; Q4: upper middle income; Q5: richest

§ Test for trend significant at $p < 0.05$