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# The prevalence, correlates and impact of anaemia among older people in Cuba, Dominican Republic, Mexico, Puerto Rico and Venezuela

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## Summary

Anaemia among older people is increasingly recognized as a matter of public health concern. Data from low- and middle-income countries are sparse. We surveyed 10915 people aged 65 years and over (8423 with blood tests) in catchment areas in Cuba, Dominican Republic, Puerto Rico, Venezuela and Mexico, to assess prevalence and correlates of anaemia and impact on disability. Prevalence varied widely between sites, from 6·4% in rural Mexico to 9·2% in urban Mexico, 9·8% in Venezuela, 19·2% in Cuba, 32·1% in Puerto Rico and 37·3% in Dominican Republic. Prevalence was higher in men and increased with age, but sociodemographic composition did not account for prevalence differences between sites. Standardized morbidity ratios indicated a much higher prevalence in Cuba (173), Puerto Rico (280) and Dominican Republic (332) compared with USA National Health and National Examination Surveys. Anaemia was associated with undernutrition, physical impairments, and serum creatinine. There was an association with greater African admixture in Dominican Republic but not in Cuba. African admixture is therefore unlikely to fully explain the high prevalence in the Caribbean islands, which may also arise from environmental, possibly dietary factors. Given an important independent contribution of anaemia to disability, more research is needed to identify preventable and treatable causes.

**Keywords:** anaemia, aged, prevalence, epidemiology, developing countries.

A recent systematic review of the prevalence of anaemia among older people identified just 34 community studies conducted since 1980, 27 of which applied World Health Organization (WHO) criteria (Gaskell *et al*, 2008). The review was confined to studies in developed countries, focusing on those predominately aged 65 years and over; very few studies have been conducted outside of North America and Europe. The weighted mean prevalence of anaemia (weighted for sample size) using the WHO definition was 12%. Prevalence was slightly higher in men than in women, and increased with age in the eight studies with age-specific estimates. In studies conducted in the USA, haemoglobin levels among older people were lower in non-Hispanic blacks compared with whites and Hispanics (Salive *et al*, 1992; Denny *et al*, 2006; Patel *et al*, 2009), and the prevalence of anaemia may be as much as three times higher (Guralnik *et al*, 2004;



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Denny *et al*, 2006). Similar findings were reported for younger adults (Perry *et al*, 1992; Beutler & West, 2005; Beutler & Waalen, 2006). In the USA National Health and National Examination Surveys (NHANES), approximately one-third of cases of anaemia in older people were adjudged to have arisen from nutritional deficiency, one-third from chronic inflammation and chronic renal failure, leaving one-third 'unexplained' (Guralnik *et al*, 2004). Despite some controversy regarding appropriate definitions for older people, there is accumulating evidence from population-based studies that anaemia is independently associated with disability, decreased physical performance and muscle strength (Penninx *et al*, 2004), and is a predictor for cognitive and physical decline (Denny *et al*, 2006), and mortality (Denny *et al*, 2006; Patel *et al*, 2009).

The 10/66 Dementia Research Group population-based studies document dementia, other chronic disease, disability and lifestyle risk factors in rural and urban catchment area sites in Latin America (Cuba, Dominican Republic, Puerto Rico, Mexico, Peru, Venezuela), India and China (Prince *et al*, 2007). Fasting blood samples were collected in a subset of Latin American sites (Cuba, Dominican Republic, Mexico, Venezuela and Puerto Rico), permitting analysis of other outcomes including anaemia, diabetes, dyslipidaemia and metabolic syndrome (Prince *et al*, 2007; Acosta *et al*, 2010). The objectives of the current analysis are to report the prevalence and social patterning of anaemia in catchment area surveys of older people in five Latin American countries, to explore the effects of undernutrition, diet, chronic disease and renal function on this outcome, and to estimate the independent contribution of anaemia to disability by extending a model previously used to estimate the independent effects of other chronic diseases and impairments across all 10/66 centres (Sousa *et al*, 2009).

## Materials and methods

One-phase population-based surveys were undertaken between 2003 and 2009, of all older people aged 65 years and over living in geographically defined catchment areas in five Latin American countries; urban sites in Cuba (Havana and Matanzas), Dominican Republic (Santo Domingo), Puerto Rico (Bayamon) and Venezuela (Caracas), and urban and rural sites in Mexico (Mexico City and Morelos province). The study protocol encompassed a detailed sociodemographic and health questionnaire, a structured clinical interview, and a physical examination including blood pressure measurement and anthropometry. An informant was interviewed for each older person. Blood samples were collected in this subset of 10/66 Dementia Research Group survey sites, allowing us to report the prevalence of anaemia and its sub-types. Studies were approved by local ethical committees and by the King's College London research ethics committee. Participation was by signed, informed consent. Those lacking capacity to consent could still participate on the basis of informed agreement of next of kin.

### *Measures*

1 Sociodemographic characteristics: age in years, sex, marital status (never married, currently married, widowed, separated or divorced), and level of education (none, did not complete primary, completed primary, secondary or tertiary).
2 Anaemia: defined according to the World Health Organization (WHO) criteria; haemoglobin levels below 130 g/l in men and 120 g/l in women. Anaemia cases were subdivided into microcytic when mean corpuscular volume (MCV) was <80 fl, normocytic when MCV was between 80 and 100 fl, and macrocytic when MCV was higher than 100 fl.
3 Potential risk factors
   a Diet; frequency of meat consumption (never, some days, most days, every day); number of portions of vegetables and fruit consumed in last 3 d
   b Nutritional status; central obesity, defined as waist circumference>101·6 cm for men, >88·9 centimetres for women; mid-upper arm circumference in centimetres [undernutrition was defined as a mid upper arm circumference of <21 cm, this cut-off point being used in the Mini Nutritional Assessment MNA® to identify the most severe level of undernutrition according to this index (Guigoz, 2006)]; serum albumin assessed from the fasting blood sample
   c Hazardous drinking, defined as a self-reported weekly intake of 21 or more units in women and 28 or more units in men.
   d Chronic disease severity; number of limiting chronic physical impairments (4c. below); self-reported 'stomach or intestine problems'; serum creatinine assessed from the fasting blood sample (only available in Cuba and Venezuela).
4 Measures of health status (used as control variables when assessing the independent contribution of anaemia to disability) comprised:
   a Directly assessed diagnoses. Dementia ascertained according to the cross-culturally validated 10/66 dementia diagnosis algorithm (Prince *et al*, 2003) and the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) dementia criterion (American Psychiatric Association, 1994); International Statistical Classification of Diseases and Related Health Problems, 10th revision (ICD-10) depressive episode (mild, moderate or severe) ascertained using the Geriatric Mental State examination (GMS) (Copeland *et al*, 2002); hypertension according to the European Society of Hypertension criteria (systolic

blood pressure $\geq$140 mm Hg and/or diastolic blood pressure $\geq$90 mm Hg, and/or a positive answer to the question 'have you ever been told by a doctor that you have hypertension?'; Chronic Obstructive Pulmonary Disease (COPD) defined as having chronic cough, productive of sputum for three or more months.

b Self-reported diagnoses; stroke, ischaemic heart disease (myocardial infarction or angina) and diabetes

c Self-reported limiting physical impairments. Self-reported paralysis, weakness or loss of a limb; eyesight problems; stomach or intestine problems; arthritis or rheumatism; heart problems; hearing difficulties or deafness; breathlessness; difficulty breathing or asthma; faint or blackouts; skin disorders such as pressure sores, leg ulcers or severe burns; persistent cough. Impairments were rated as present if they interfered with activities 'a little' or 'a lot' (George & Fillenbaum, 1985).

5 Disability was measured using the 12–item WHO Disability Assessment Schedule version 2.0 (WHODAS 2.0) (World Health Organization, 2010). There are five activity limitation domains, each with two questions: understanding/communication, getting around (mobility), self-care, getting along with people (interpersonal interaction) and life activities. A sixth domain, participation in society, assesses broader social aspects of disability. WHODAS 2.0 has high internal consistency, moderate to good test-retest reliability, and good concurrent validity in many different chronic disease clinical populations. We demonstrated cross-cultural validity and measurement invariance across the 10/66 Dementia Research Group population-based surveys (Sousa *et al*, 2010).

### *Analyses*

All analyses were carried out in STATA 9.2 (Statacorp, College Station, TX, USA) using the 10/66 blood test merged dataset version 2.0.

1 We describe the socio-demographic characteristics, diet, nutritional status, behavioural risk factors, prevalence of chronic diseases and impairments, and median disability scores among those who provided a blood sample.

2 We report the prevalence of anaemia by age and sex with standard errors and robust 95% confidence intervals (CIs), taking into account household clustering. We used direct standardization to compare the prevalence of anaemia between sites, standardizing for compositional differences in age, sex, education and assets using the whole pooled sample as the standard population. We compared the prevalences of anaemia in each site with those from the US NHANES III (Guralnik *et al*, 2004) using indirect standardization to generate age- and sex-standardized morbidity ratios (SMR) with mid-point 95% CIs.

3 We modelled the effects of age, sex, education and assets, providing mutually adjusted prevalence ratios (PRs) with 95% CIs, derived from a poisson working model. We fitted the model separately for each site and then combined estimates using fixed effect meta-analysis, estimating the degree of heterogeneity using Higgins $I^2$ and approximate 95% CIs.

4 Two sets of Poisson models were fitted to test for correlates of anaemia. First, we estimated associations between anaemia and dietary meat intake, dietary vegetable intake, albumin, arm circumference, hazardous alcohol consumption, number of chronic physical impairments, self-reported gastrointestinal impairment, and creatinine, controlling for age, sex, education and assets. Next, we estimated the same associations mutually controlling for all other risk factors. However, to avoid collinearity and over adjustment (i) albumin was not controlled for arm circumference and *vice versa*, (ii) other risk factors were controlled for albumin but not arm circumference, (iii) gastrointestinal impairment was controlled for number of chronic physical impairments omitting gastrointestinal impairment and (iv) chronic physical impairment was not controlled for gastrointestinal impairment. We used fixed effect meta-analysis to combine PRs generated from the second model.

5 We tested for an independent effect of anaemia on disability by extending models previously used to estimate independent effects of other health disorders (Sousa *et al*, 2009) to include the effect of anaemia. First, we generated zero-inflated negative binomial models, separately for each site, to estimate the independent associations of anaemia with WHODAS 2.0 score counts (count ratios), controlling for other health disorders, age, sex, education, and marital status. This modelling approach provides optimal goodness of fit for the observed WHODAS 2.0 distributions, estimating the effect of covariates on the count score, controlling for their effect on excess zeros, while also addressing over dispersion (the higher than expected proportion of relatively high disability scores; Sousa *et al*, 2009). We then fitted the same models using a Poisson regression working model with the 90th centile of the WHODAS 2.0 distribution in each site as a threshold; the aim being to calculate a population-attributable prevalence fraction (PAPF) for the independent association between anaemia and high disability scores, using the Stata aflogit command. The PAPF reflects the potential reduction in prevalence of high disability scores if the health conditions concerned could be removed from the population, accounting for the prevalence of the health conditions, and their effects on the prevalence of severe disability (a product of their effects upon onset and duration), assuming that the associations were causal and estimated free of confounding.

6 In the Cuban survey the interviewer's perception of the participant's ethnic identity was coded according to categories used in the Cuban census – 'Blanco – white', 'Mestizo – mixed' and 'Negro – black'. We compared mean haemoglobin, the prevalence of anaemia, mean

systolic blood pressure and serum creatinine levels between these three groups. We had also previously estimated admixture (the proportion of an individual's genome that has ancestry from African, European and native American founding populations) in Cuba and Dominican Republic by genotyping 60 single nucleotide polymorphisms with an average 40% information content for ancestry, sufficient to estimate three-way individual admixture proportions with a standard error of <0·1 (Smith *et al*, 2004). The ADMIXMAP program (Hoggart *et al*, 2004) (http://homepages.ed.ac.uk/pmckeigu/admixmap/) was used to generate posterior means of individual admixture from the ancestry informative marker data. In these sites, characterized by high levels of European/African admixture we estimated the main effect of admixture (100% African *versus* 100% European) on mean haemoglobin, systolic blood pressure and creatinine, controlling for age, sex and education. For the Cuban sample, where genotyping was conducted on 235 dementia cases and 349 randomly selected controls free from dementia, sample weights were used to weight back for the probability of selection by dementia case and control status and APOE genotype (Teruel *et al*, 2011).

## Results

There were 10 915 participants in the baseline surveys in the subset of six Latin American 10/66 Dementia Research Group survey sites in which blood samples were taken and analysed for haemoglobin. Response rates for the survey varied between 80% and 95%. Overall, 8423 blood samples were collected. By site, the numbers and proportions providing samples were: Cuba (2355, 80·4% of those participating in the survey), Dominican Republic (1483, 73·8%), Puerto Rico (1584, 78·8%), Venezuela (1284, 65·3%), urban Mexico (822, 82·0%), and rural Mexico (895, 89·5%). There were few differences in baseline characteristics of those who did and did not provide samples (Table I), and those that were statistically significant were generally of small effect. Older participants were slightly less likely to provide samples in Cuba, and males were slightly less likely to provide samples in Cuba and Dominican Republic. Better educated participants were slightly more likely to provide samples in Cuba, Puerto Rico and urban Mexico. Chronic diseases and disability were underrepresented among those that provided samples in Puerto Rico and urban Mexico. The characteristics, by site, of survey participants who provided blood samples are described in Table II. Mean age varied from 72·6 years in Venezuela to 75·7 years in Puerto Rico. Women predominated over men in all sites accounting for between 60·4% and 68·1% of participants. Participants in Dominican Republic and rural Mexico stood out as being relatively disadvantaged with lower educational levels, fewer household assets, and a higher prevalence of food insecurity. Fish dominated participants' diets in Venezuela, in marked contrast to the meat-based diets in Cuba and Dominican Republic. Relatively few Mexican participants reported regularly eating either meat or fish. Vegetable consumption was lower in Dominican Republic, Puerto Rico,

**Table I.** Associations (prevalence ratios with 95% confidence intervals) between sociodemographic, health and lifestyles factors and consenting to provide a blood sample, by site.

| | Cuba | Dominican Republic | Puerto Rico | Venezuela | Mexico, urban | Mexico, rural |
|---|---|---|---|---|---|---|
| Age (per 5 year band) | **0·98 (0·96–1·00)** | 0·99 (0·97–1·02) | 0·99 (0·97–1·02) | 1·01 (0·98–1·04) | 0·98 (0·95–1·01) | 1·00 (0·98–1·02) |
| Sex (male *versus* female) | **0·97 (0·93–1·00)** | **0·91 (0·86–0·96)** | 0·98 (0·94–1·02) | 0·97 (0·91–1·03) | 0·96 (0·90–1·01) | 0·99 (0·96–1·03) |
| Education (per level) | **1·02 (1·01–1·04)** | 0·99 (0·96–1·02) | **1·04 (1·02–1·06)** | 0·99 (0·96–1·03) | **1·04 (1·01–1·07)** | 1·01 (0·98–1·03) |
| Assets (per quarter) | 1·02 (1·00–1·04) | 0·99 (0·96–1·02) | **1·05 (1·02–1·08)** | 0·98 (0·94–1·01) | **1·05 (1·02–1·07)** | 1·01 (0·99–1·03) |
| Married | 1·01 (0·98–1·05) | 1·01 (0·95–1·08) | **1·07 (1·02–1·13)** | 1·02 (0·96–1·10) | 1·03 (0·97–1·10) | 1·01 (0·96–1·05) |
| Ever smoked | 0·98 (0·95–1·02) | 0·98 (0·93–1·03) | 0·96 (0·91–1·01) | 1·01 (0·94–1·07) | 0·95 (0·90–1·01) | 1·00 (0·96–1·05) |
| Arm circumference (per SD) | 1·01 (0·99–1·03) | 1·02 (0·99–1·04) | **1·02 (1·01–1·04)** | 1·00 (0·96–1·04) | 0·98 (0·94–1·02) | 0·98 (0·95–1·01) |
| Obese (meets metabolic syndrome criteria) | 1·01 (0·98–1·05) | **1·08 (1·02–1·13)** | 1·01 (0·98–1·04) | 1·03 (0·96–1·09) | 1·00 (0·94–1·06) | 0·97 (0·93–1·01) |
| ICD-10 Depression | 1·00 (0·92–1·09) | **1·10 (1·03–1·17)** | 0·89 (0·74–1·07) | 0·94 (0·81–1·09) | 0·96 (0·82–1·12) | 1·02 (0·91–1·14) |
| Dementia | 1·00 (0·94–1·06) | 0·97 (0·90–1·06) | **0·68 (0·60–0·77)** | 0·94 (0·83–1·08) | 0·91 (0·81–1·03) | 0·97 (0·89–1·06) |
| Stroke | 1·01 (0·95–1·08) | 1·01 (0·92–1·10) | **0·88 (0·80–0·97)** | 1·00 (0·88–1·13) | 0·92 (0·80–1·06) | **1·06 (1·00–1·13)** |
| Ischaemic heart disease | 0·96 (0·90–1·01) | 0·90 (0·75–1·07) | 0·91 (0·82–1·01) | 0·95 (0·82–1·09) | 0·90 (0·74–1·10) | 1·04 (0·91–1·20) |
| Hypertension | 1·03 (0·99–1·08) | 1·03 (0·96–1·10) | **0·92 (0·87–0·96)** | 0·94 (0·87–1·01) | 0·97 (0·91–1·02) | 1·01 (0·96–1·05) |
| Number of physical impairments | 1·01 (1·00–1·03) | **1·03 (1·01–1·04)** | **0·98 (0·96–0·99)** | 1·00 (0·98–1·01) | **0·97 (0·95–1·00)** | 1·01 (1·00–1·02) |
| Severe disability (above the 90th centile for WHODAS 2.0) | 0·98 (0·92–1·05) | 0·98 (0·89–1·08) | **0·71 (0·63–0·80)** | 1·03 (0·93–1·14) | **0·80 (0·69–0·94)** | 1·00 (0·93–1·08) |

SD, standard deviation; ICD-10, International Classification of Diseases, version 10; WHODAS 2.0, World Health Organization Disability Assessment Schedule version 2.0.

Prevalence ratios in bold type indicate a statistically significant association at $P < 0.05$.

**Table II.** Socio-demographic characteristics and prevalence of health conditions.

| | Cuba | Dominican Republic | Puerto Rico | Venezuela | Mexico, urban | Mexico, Rural |
|---|---|---|---|---|---|---|
| Total sample (% response) | 2928 (94) | 2010 (95) | 2009 (93) | 1965 (80) | 1003 (84) | 1000 (86) |
| Numbers providing a blood sample (% of total sample) | 2355 (80·4) | 1483 (73·8) | 1584 (78·8) | 1284 (65·3) | 822 (82·0) | 895 (89·5) |
| Sociodemographic characteristics | | | | | | |
| Age in years, mean (SD) | 75·0 (7·1) | 75·0 (7·3) | 75·7 (7·1) | 72·6 (6·8) | 74·2 (6·4) | 74·1 (6·6) |
| Sex (female %) | 1549 (65·9) | 1008 (68·1) | 1070 (67·8) | 776 (65·0) | 554 (67·4) | 539 (60·4) |
| Currently married (%) | 1017 (43·4) | 437 (29·7) | 789 (50·0) | 572 (48·2) | 391 (47·6) | 482 (54·0) |
| Did not complete primary education (%) | 570 (24·3) | 1047 (71·2) | 333 (21·0) | 360 (30·3) | 462 (56·3) | 749 (83·9) |
| Median assets (25th and 75th centiles) | 6 (5–6) | 5 (4–6) | 7 (6–7) | 6 (6–7) | 6 (6–7) | 4 (3–6) |
| Diet, nutritional status, and behavioural risk factors | | | | | | |
| Meat consumption most or every day (%) | 1076 (36·9) | 1094 (55·0) | 567 (35·9) | 253 (14·5) | 235 (23·6) | 145 (14·5) |
| Fish consumption most or every day (%) | 243 (10·3) | 118 (8·0) | 28 (1·8) | 565 (47·5) | 61 (7·5) | 18 (2·0) |
| Median portions of vegetables consumed in last 3 d (25th and 75th centiles) | 4 (3–6) | 3 (1–4) | 3 (2–6) | 3 (3–6) | 4 (3–6) | 3 (2–4) |
| Food insecurity (%) | 108 (4·6) | 185 (12·6) | 23 (1·5) | 71 (6·2) | 34 (4·2) | 74 (8·4) |
| Arm circumference (cm) (mean, SD) | 27·5 (5·2) | 31·1 (6·8) | 29·9 (5·1) | 28·6 (6·0) | 26·9 (4·3) | 24·7 (3·5) |
| Arm circumference <21 cm (%) | 108 (4·6) | 38 (2·6) | 33 (2·3) | 21 (1·9) | 16 (2·0) | 67 (7·5) |
| Albumin (<35 g/l) (%) | 236 (11·1) | 122 (8·9) | Not assessed | 46 (3·6) | 8 (1·0) | 30 (3·4) |
| Obese | 860 (36·8%) | 700 (47·6%) | 780 (54·5) | 515 (48·1%) | 466 (57·2%) | 356 (40·3%) |
| Ever smoked | 1045 (44·6%) | 700 (47·3%) | 420 (26·6%) | 517 (43·7%) | 282 (34·3%) | 243 (27·2%) |
| Hazardous drinking (%) | 90 (3·8) | 164 (11·1) | 16 (1·0) | 7 (1·0) | 5 (0·6) | 10 (1·0) |
| Chronic diseases and impairments | | | | | | |
| Dementia | 257 (10·9%) | 173 (11·7%) | 130 (8·2%) | 86 (7·1%) | 70 (8·5%) | 75 (8·4%) |
| Stroke | 186 (7·9%) | 130 (8·8%) | 118 (7·5%) | 90 (7·6%) | 51 (6·2%) | 70 (7·8%) |
| Hypertension | 1733 (73·7%) | 1130 (76·2%) | 1207 (78·4%) | 938 (77·5%) | 546 (66·4%) | 488 (54·6%) |
| Self-reported ischaemic heart disease (myocardial infarction or angina) | 316 (13·5%) | 40 (2·7%) | 111 (7·0%) | 75 (6·3%) | 29 (3·5%) | 14 (1·6%) |
| Self-reported gastrointestinal impairment (%) | 215 (9·2) | 303 (20·5) | 317 (20·1) | 220 (18·5) | 100 (12·2) | 158 (17·7) |
| Number of limiting physical impairments (%) | | | | | | |
| None | 1010 (43·1) | 407 (27·5) | 577 (36·5) | 465 (38·9) | 383 (46·6) | 339 (38·0) |
| 1–2 | 1102 (47·0) | 724 (48·9) | 679 (42·9) | 420 (35·2) | 314 (38·2) | 386 (43·2) |
| 3 or more | 233 (9·9) | 350 (23·6) | 325 (20·6) | 309 (25·9) | 125 (15·2) | 168 (18·8) |
| Median WHODAS 2.0 score (25th and 75th centiles) | 5·6 (0–19·4) | 8·3 (0–27·8) | 5·6 (0·0–22·2) | 2·8 (0–13·9) | 2·8 (0–11·1) | 0 (0–13·9) |

SD, standard deviation; WHODAS 2.0, World Health Organization Disability Assessment Schedule version 2.0.

Venezuela and rural Mexico. In terms of hypoalbuminaemia, undernutrition was most marked in Cuba and Dominican Republic, while small arm circumferences were most prevalent in Cuba and rural Mexico. Hazardous drinking was unusual, other than in the Dominican Republic. Dementia (7–12% by site), stroke (6–9%) and hypertension (55–78%) were all quite highly prevalent. The wide variation in self-reported ischaemic heart disease diagnoses may have reflected differences in levels of awareness, and access to health services. WHODAS 2.0 disability scores were somewhat higher in Cuba, Dominican Republic and Puerto Rico compared with other sites.

### *The prevalence of anaemia*

Cuba (19·2%), Puerto Rico (32·1%), and Dominican Republic (37·3%) stood out as having a particularly high prevalence of anaemia (Table III). Mean haemoglobin levels were around 10 g/l lower in Cuba, 15 g/l lower in Puerto Rico and 20 g/l lower in Dominican Republic compared with Mexico (Table III). The prevalence of anaemia increased with age in all sites (meta-analysed PR per 5 year age band 1·03, 95% CI 1·02–1·03; Table IV). Mean haemoglobin levels were approximately 10 g/l lower in women than men across all sites (Table III) and prevalence was higher in men than in women (meta-analysed PR 1·35, 1·22–1·48), particularly in the oldest age group (Tables III and IV). There was a less consistent tendency for anaemia to be concentrated in those of lower socioeconomic status, the inverse associations with assets being more prominent in Cuba and Dominican Republic. Direct standardization for the effects of these compositional factors had little effect on the pattern of prevalence between sites, with Cuba, Dominican Republic and Puerto Rico still standing out as having a particularly high prevalence (Table III). Following

**Table III.** Prevalence of anaemia by site, age and sex, and standardized prevalence*.

| Site | Sex | Mean haemoglobin, g/l (SD) | Prevalence (% with 95% confidence intervals), by age | | | | | Total prevalence (95% confidence intervals) | Direct standardization – Standardized Prevalence* (95% confidence intervals) | Indirect standardization-Standardized morbidity ratio (95% confidence intervals) |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | 65–69 | 70–74 | 75–89 | 80+ | All ages | | | |
| Cuba | Female | 133 (14) | 10·7% (7·7–13·7) | 14·6% (11·2–18·0) | 13·0% (9·3–16·7) | 25·8% (21·3–30·2) | 16·0% (14·2–17·9) | 19·2% (17·6–20·9) | 16·9% (15·4–18·4) | 173 (157–189) |
| | Male | 141 (15) | 17·2% (12·0–22·3) | 19·5% (14·4–24·5) | 24·7% (18·2–31·2) | 43·1% (35·9–50·3) | 25·4% (22·4–28·5) | | | |
| Dominican Republic | Female | 124 (13) | 34·0% (28·3–39·6) | 27·4% (21·9–33·0) | 40·0% (33·2–46·8) | 40·6% (34·9–46·2) | 35·4% (32·5–38·4) | 37·3% (34·9–39·8) | 31·8% (29·1–34·6) | 332 (305–361) |
| | Male | 133 (16) | 31·3% (23·4–39·2) | 35·9% (27·7–44·1) | 44·0% (33·8–54·2) | 56·3% (47·4–65·2) | 41·3% (36·8–45·8) | | | |
| Puerto Rico | Female | 130 (14) | 18·6% (13·5–23·6) | 21·9% (16·7–27·2) | 22·6% (17·6–27·7) | 22·1% (17·6–26·5) | 21·4% (19·0–23·9) | 32·1% (29·9–34·3) | 24·9% (22·8–26·9) | 280 (256–305) |
| | Male | 130 (14) | 51·8% (41·0–62·6) | 58·8% (50·0–67·7) | 50·7% (42·4–59·1) | 54·4% (47·1–61·7) | 54·0% (49·8–58·3) | | | |
| Venezuela | Female | 136 (12) | 6·7% (4·0–9·4) | 6·0% (2·4–9·6) | 12·8% (7·3–18·3) | 15·9% (9·5–22·3) | 9·2% (7·1–11·2) | 9·8% (8·1–11·5) | 7·0% (5·8–8·3) | 101 (84–120) |
| | Male | 148 (14) | 6·8% (3·1–10·5) | 8·7% (3·3–14·2) | 9·0% (2·6–15·3) | 22·6% (11·4–33·9) | 9·8% (6·9–12·6) | | | |
| Urban Mexico | Female | 147 (17) | 3·9% (0·9–7·0) | 8·3% (4·3–12·4) | 6·6% (1·9–11·3) | 4·5% (0·6–8·4) | 6·0% (4·1–10·4) | 6·4% (4·7–8·1) | 4·1% (3·0–5·2) | 59 (45–77) |
| | Male | 159 (19) | 4·3% (0·0–10·0) | 6·2% (1·4–11·0) | 1·7% (0·0–5·0) | 16·7% (7·2–26·1) | 7·2% (4·1–10·4) | | | |
| Rural Mexico | Female | 144 (17) | 4·5% (1·5–7·6) | 8·3% (3·6–13·0) | 7·2% (2·7–11·7) | 10·6% (4·7–16·4) | 7·2% (5·1–9·4) | 9·2% (7·3–11·1) | 6·4% (4·5–8·2) | 85 (68–104) |
| | Male | 153 (2) | 5·5% (0·8–10·2) | 13·5% (6·3–20·6) | 13·0% (5·5–20·5) | 16·7% (9·2–24·1) | 12·1% (8·8–15·6) | | | |

*Standardized for age, sex, education and assets.
SD, standard deviation.

**Table IV.** Social patterning of anaemia – associations (mutually adjusted prevalence ratios with 95% confidence intervals) between anaemia and age, sex, education and household assets, by site.

| | Age (per 5-year band) | Sex M *versus* F | Education (per level) | Assets (per quarter) |
|---|---|---|---|---|
| Cuba | 1·05 (1·04–1·06) | 1·65 (1·41–1·95) | 1·02 (0·93–1·09) | 0·88 (0·81–0·96) |
| Dominican Republic | 1·02 (1·02–1·03) | 1·19 (1·04–1·36) | 0·97 (0·91–1·04) | 0·86 (0·80–0·92) |
| Puerto Rico | 1·02 (0·96–1·09) | 2·51 (2·18–2·90) | 1·00 (0·94–1·07) | 1·00 (0·92–1·09) |
| Venezuela | 1·06 (1·04–1·08) | 1·08 (0·74–1·57) | 1·03 (0·83–1·26) | 0·99 (0·83–1·21) |
| Urban Mexico | 1·04 (0·99–1·07) | 1·17 (0·67–2·04) | 0·79 (0·59–1·05) | 1·19 (0·96–1·48) |
| Rural Mexico | 1·04 (1·01–1·06) | 1·62 (1·08–2·42) | 0·86 (0·65–1·13) | 1·16 (0·96–1·41) |
| Meta-analysed PR (95% CI) | 1·03 (1·02–1·03) | 1·35 (1·22–1·48) | 0·92 (0·94–1·03) | 0·91 (0·86–0·95) |
| Cochran's Q | 40·2 | 11·7 | 4·3 | 15·9 |
| Higgins $I^2$ (96% CI) | 90 (80–95) | 66 (10–87) | 7 (0–81) | 75 (38–90) |

M, male; F, female; PR, prevalence ratio; CI, confidence interval.

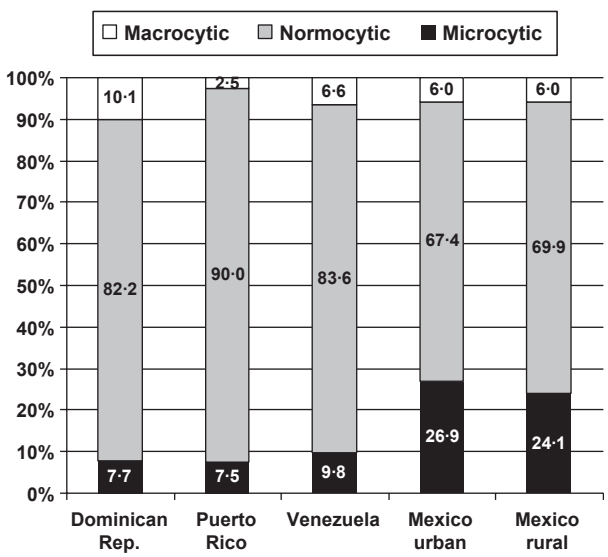


**Fig 1.** Proportion of anaemia cases that are macrocytic, normocytic and microcytic, by 10/66 site.

indirect standardization, applying age- and sex–specific prevalences from NHANES III, standardized morbidity ratios (SMR) suggested a greater than three times higher prevalence in Dominican Republic compared with the USA, a 2·8 times higher prevalence in Puerto Rico, a 1·7 times higher prevalence in Cuba, a similar prevalence in Venezuela, and a somewhat lower prevalence in Mexico (Table III).

In all sites, the commonest type of anaemia was normocytic (Fig 1). However, microcytic anaemia was more than twice as common in Mexico (accounting for 26·9% of cases in the urban, and 24·1% in the rural catchment areas) than in other sites (7·5–9·8%).

### *Associations between potential risk factors and anaemia as an outcome*

Table V describes the associations between anaemia and hypothesized chronic disease and nutritional risk factors after adjusting for age, sex, education and assets. There was strong evidence for an effect of undernutrition, with inverse associations between meat intake (meta-analysed PR per frequency category 0·91, 0·85–0·96), serum albumin (meta-analysed PR per standard deviation (SD) 0·82, 0·77–0·85) and arm circumference (meta-analysed PR per SD 0·76, 0·71–0·81). Vegetable intake was not associated with anaemia prevalence, other than in Venezuela. There were no significant associations between hazardous drinking and anaemia in any site; the meta-analysed tendency was towards a protective effect (PR 0·82, 0·66–1·01). Numbers of chronic physical impairments were generally associated with anaemia, although the effects were attenuated after controlling for other risk factors (final adjusted meta-analysed PR 1·08, 1·02–1·14). Renal function (serum creatinine) was only assessed in Cuba, Puerto Rico and Venezuela, but in these sites there was a strong effect with higher creatinine levels being positively associated with anaemia (meta-analysed PR per SD 1·17, 1·14–1·20).

In Cuba, there was no association between interviewer perception of ethnicity and the prevalence of anaemia; 18·4% in those considered 'white', 23·8% in those considered 'mixed' and 20·3% in those considered 'black' (Chi-square test for trend = 1·7, $P = 0·20$). Mean haemoglobin was just 1·0 g/l lower in 'black' than 'white' participants after controlling for age, sex and education (Table VI). Serum creatinine levels were higher in participants considered 'black'. There was no association between individual admixture and either haemoglobin level, systolic blood pressure or serum creatinine. However, in the Dominican Republic haemoglobin levels were estimated to be 6·0 g/l (95% CI 3·0–9·0) lower in those with 100% African admixture compared with those with 100% Caucasian admixture, with a PR for anaemia of 2·49 (95% CI 1·53–4·03). Blood pressure levels were also estimated to be higher in those with 100% African admixture (mean difference 5·1 mmHg, 95% CI 0·6–9·6).

### *Anaemia as an independent contributor to disability*

Accounting for zero inflation, and controlling for other chronic diseases and impairments, WHODAS 2.0 disability score

**Table V.** Poisson regression (adjusted prevalence ratios) for the associations between anaemia and hypothesized chronic disease and nutritional risk factors.

| Exposure | Model | Cuba | Dominican Republic | Puerto Rico | Venezuela | Urban Mexico | Rural Mexico | Meta-analysed (PR) | Cochrane Q Higgins $I^2$ (95% CI)* |
|---|---|---|---|---|---|---|---|---|---|
| Dietary meat intake (per frequency category) | 1 | 0·90 (0·80–1·02) | 0·96 (0·90–1·04) | 1·00 (0·93–1·09) | 0·83 (0·61–1·15) | 0·80 (0·52–1·22) | 0·55 (0·37–0·83) | 0·94 (0·89–0·99) | 7·0, 5 df |
| | 2 | 0·89 (0·78–1·02) | 0·98 (0·90–1·06) | 0·95 (0·87–1·05) | 0·84 (0·64–1·11) | 0·85 (0·53–1·36) | 0·62 (0·42–0·91) | | 28% (0–70) |
| No meat in diet | 1 | 1·14 (0·76–1·69) | 1·06 (0·81–1·38) | 0·97 (0·73–1·29) | 1·51 (1·00–2·26) | 1·12 (0·47–2·71) | 1·91 (1·13–3·24) | 1·16 (0·99–1·36) | 6·5, 5 df |
| | 2 | 1·00 (0·63–1·59) | 1·03 (0·77–1·37) | 1·06 (0·80–1·40) | 1·84 (1·15–2·94) | 1·16 (0·46–2·93) | 1·58 (0·93–2·68) | | 23% (0–67) |
| Dietary vegetable intake (per additional portion over 3 d) | 1 | 1·11 (1·02–1·19) | 0·92 (0·85–0·98) | 1·01 (0·99–1·04) | 1·02 (0·83–1·25) | 1·12 (0·87–1·44) | 1·23 (1·02–1·48) | 1·01 (0·99–1·02) | 21·2, 5 df |
| | 2 | 1·01 (0·99–1·04) | 0·99 (0·97–1·02) | 0·99 (0·96–1·03) | 0·91 (0·84–0·97) | 0·99 (0·95–1·04) | 1·08 (1·03–1·12) | | 76% (47–89) |
| Albumin (per SD) | 1 | 0·87 (0·80–0·96) | 0·97 (0·90–1·04) | Not assessed | 0·60 (0·51–0·70) | 0·48 (0·42–0·56) | 0·54 (0·47–0·61) | 0·82 (0·77–0·85) | 105·5, 4 df |
| | 2 | 0·88 (0·80–0·96) | 0·97 (0·91–1·04) | Not assessed | 0·61 (0·52–0·70) | 0·50 (0·42–0·59) | 0·54 (0·47–0·63) | | 96% (93–38) |
| Arm circumference (per SD) | 1 | 0·78 (0·69–0·89) | 0·78 (0·72–0·84) | 0·94 (0·87–1·02) | 0·93 (0·61–1·41) | 1·02 (0·70–1·48) | 0·52 (0·38–0·71) | 0·81 (0·76–0·85) | 19·6, 5 df |
| | 2 | 0·75 (0·65–0·86) | 0·76 (0·70–0·82) | 0·93 (0·86–1·05) | 0·96 (0·66–1·39) | 1·01 (0·67–1·51) | 0·53 (0·39–0·74) | | 74% (42–89) |
| Hazardous alcohol consumption | 1 | 0·81 (0·50–1·30) | 0·79 (0·63–1·00) | 0·97 (0·64–1·46) | 1·62 (0·25–10·58) | – | 0·87 (0·13–5·79) | 0·82 (0·66–1·01) | 0·6, 4 df |
| | 2 | 0·82 (0·50–1·36) | 0·79 (0·62–1·01) | 1·08 (0·42–2·76) | 1·03 (0·12–9·14) | – | 1·13 (0·26–4·97) | | 0% (0–79) |
| Number of chronic physical impairments | 1 | 1·10 (0·98–1·25) | 1·11 (1·01–1·22) | 0·95 (0·86–1·04) | 1·00 (0·80–1·25) | 1·40 (1·03–1·90) | 1·23 (0·93–1·60) | 1·08 (1·02–1·14) | 0·9, 5 df |
| | 2 | 1·09 (0·95–1·24) | 1·10 (0·99–1·21) | 1·06 (0·96–1·18) | 1·00 (0·80–1·26) | 1·16 (0·83–1·64) | 1·07 (0·80–1·43) | | 0% (0–75) |
| Self-reported gastrointestinal impairment | 1 | 0·89 (0·66–1·20) | 1·05 (0·90–1·24) | 1·03 (0·87–1·21) | 0·75 (0·45–1·23) | 1·24 (0·60–2·59) | 1·40 (0·85–2·28) | 1·00 (0·89–1·11) | 3·6, 5 df |
| | 2 | 0·97 (0·71–1·31) | 1·00 (0·84–1·20) | 1·02 (0·85–1·22) | 0·63 (0·37–1·07) | 1·28 (0·62–2·66) | 1·12 (0·69–1·82) | | 0% (0–75) |
| Creatinine (per SD) | 1 | 1·10 (1·21–1·44) | Not assessed | 1·18 (1·14–1·22) | 1·19 (1·13–1·24) | Not assessed | Not assessed | 1·17 (1·14–1·20) | 3·9, 2 df |
| | 2 | 1·09 (1·01–1·17) | Not assessed | 1·18 (1·14–1·22) | 1·18 (1·12–1·25) | Not assessed | Not assessed | | 49% (0–85) |

[1]Controlling for age, sex, education and assets.

[2]Controlling for age, sex, education, assets, and all other variables in the table, other than that (i) albumin is not controlled for arm circumference and *vice versa*, (ii) other variables are controlled for albumin but not arm circumference, (iii) chronic physical impairment is not controlled for gastrointestinal (GI) impairment and (iv) GI impairment is controlled for number of chronic physical impairments omitting GI impairment.

*Higgins $I^2$ not calculated for meta-analysed creatinine estimates due to small number of degrees of freedom (df).

Prevalence ratios in bold type indicate a statistically significant association at $P < 0.05$.

SD, standard deviation; PR, prevalence ratio; CI, confidence interval.

**Table VI.** The effect of interviewer perception of ethnicity (Cuba), and genetic admixture (Cuba and Dominican Republic), upon haemoglobin, systolic blood pressure and serum creatinine.

| | | Interviewer perception of ethnicity (Cuba) | | | | | Effect of admixture (100% African *versus* 100% European genetic admixture)* | |
|---|---|---|---|---|---|---|---|---|
| | | White ($N$ = 1634) | Mixed ($N$ = 260) | Black ($N$ = 380) | Test for trend across three categories ($P$ = value) | 'Black' *versus* 'white' (interviewer perception – full sample) | Cuba (sub-sample) | Dominican Republic |
| Haemoglobin (g/l) | Crude mean (SD) | 136 (14) | 133 (14) | 134 (15) | $F$ = 6·3 (0·012) | | Anaemia, adjusted* prevalence ratio 0·96 (0·41–2·26) | Anaemia, adjusted* prevalence ratio 2·49 (1·53–4·03) |
| | Adjusted* marginal means | 137 | 134 | 135 | $F$ = 6·1 (0·014) | −1 (−3 to 0) | −2 (−8 to +4) | −6 (−9 to −3) |
| Systolic blood pressure (mmHg) | Crude mean (SD) | 145·4 (25·8) | 144·5 (25·0) | 148·3 (25·5) | $F$ = 3·2 (0·07) | | | |
| | Adjusted* marginal means | 145·2 | 144·2 | 147·8 | $F$ = 2·3 (0·13) | +2·6 (−0·2 to +5·4) | −9·5 (−20·7 to +1·6) | +5·1 (+0·6 to +9·6) |
| Serum creatinine (μmol/l) | Crude mean (SD) | 81·3 (26·1) | 84·1 (29·9) | 85·9 (25·5) | $F$ = 9·5 (0·002) | | | |
| | Adjusted* marginal means | 83·3 | 85·7 | 89·0 | $F$ = 13·5 (<0·001) | +5·7 (+2·6 to +8·8) | +8·4 (−7·9 to +24·7) | Not assessed |

SD, standard deviation.
*Adjusted for age, sex and educational level.

counts were consistently higher among those with anaemia; 12% higher in Cuba (count ratio 1·12, 95% CI 1·01–1·23), 13% higher in Dominican Republic (1·13, 1·04–1·24), 12% higher in Puerto Rico (1·12, 1·02–1·24), 28% higher in Venezuela, (1·28, 1·07–1·54), 15% higher in urban Mexico (1·15, 0·91–1·46) and 27% higher in rural Mexico (1·27, 1·02–1·59). The population attributable prevalence fractions for the independent association between anaemia and severe disability (above the 90th centile for WHODAS 2.0 score) were 8·3% (95% CI 5·2–11·3) in Cuba, 6·5% (0·0–14·4) in Dominican Republic, 16·8% (8·0–24·8) in Puerto Rico, 9·4% (0·6–17·5) in Venezuela, and 4·6% (0·7–8·4) in rural Mexico. The association with severe disability was null in urban Mexico.

## Discussion

To our knowledge, these are the first estimates of the prevalence of anaemia among older people in Latin America, and among the first epidemiological studies from less developed countries, where the social protection of older people is not always assured, and undernutrition can be a significant problem. Our surveys had reasonably large sample sizes and good response rates, with little evidence of response bias. A significant limitation, given the catchment area design, is that we cannot generalize our findings to the countries in which the research was conducted. We selectively sampled catchment areas that were typical of the modest socioeconomic status that prevailed in Havana, Santo Domingo, Bayamon, Caracas, Mexico City and Morelos province. We found a wide variation in the prevalence of anaemia, from levels that were lower (Mexico) or similar (Venezuela) to those reported in the nationally representative USA NHANES III, ranging up to those that were two to three times higher (Cuba, Dominican Republic and Puerto Rico).

While older age, male sex and lower socioeconomic position were associated with a higher prevalence of anaemia, these compositional variables did not account for the observed difference in prevalence between sites. The main correlates of anaemia were indices of undernutrition (limited meat intake, small arm circumference, low albumin), although chronic physical impairments and high creatinine levels (in Cuba, Puerto Rico and Venezuela, where this exposure was assessed) were also associated. There was no evidence for any significant impact of hazardous drinking or gastrointestinal impairment.

It would be tempting to conclude that high levels of African admixture in the three Caribbean sites, Cuba, Dominican Republic and Puerto Rico, may have accounted for their high prevalence of anaemia. However, in Cuba, the differences in haemoglobin level between ethnic groups, while statistically significant, were much smaller than the 4·0 to 14 g/l reported in the USA (Patel *et al*, 2009), and there was no effect of African admixture on haemoglobin level or anaemia risk. However, in Dominican Republic we estimated haemoglobin to be 6·0 g/l lower, and anaemia risk to be 2·5 times higher in those with 100% African *versus* those with 100% European ancestry. While there were small differences between Cuban interviewer-defined racial groups on systolic blood pressure and creatinine levels, these did not appear to be determined by genetic ancestry. There was a significant trend towards higher systolic blood pressure level with greater African admixture in the Dominican Republic. Notwithstanding the large contribution of the alpha thalassemia deletion in the US (Beutler & West, 2005), our findings raise the possibility that some of the interracial differences in haemoglobin level found in the USA may have arisen from sub-cultural differences in environmental exposures, possibly in interaction with genes linked to ancestry. Cuban and Dominican Republic populations are both more admixed than the USA. Cuba, post-1958, is more societally homogenous with respect to education, diet and socioeconomic status.

Undernutrition may have explained some of the excess of anaemia in Cuba and the Dominican Republic. The Cuban diet is limited, but balanced. Most participants reported a regular meat intake, and food insecurity was comparatively uncommon in our sample. However, undernutrition as indexed by arm circumference is quite prevalent. The Dominican Republic site is characterized by particularly high levels of food insecurity, low levels of education and a lack of social protection for older people. However, the rural Mexican site was similarly underdeveloped but the prevalence of anaemia there was relatively low. More detailed information on dietary components, and biomarkers for specific micronutrients might help to explain these inconsistencies. Lack of information, in our study, regarding serum iron, transferrin, ferritin, free erythrocyte protoporphyrin, folate and vitamin $B_{12}$ meant that we were not able to distinguish anaemia linked to specific nutritional deficiencies from anaemia of chronic inflammation. As others have concluded, more detailed clinical appraisal is indicated to further distinguish blood loss from nutritional iron deficiency, and to identify myelodysplasia and haematological malignancies (Pang & Schrier, 2012). Longitudinal research is required to establish which correlates of anaemia may be potentially modifiable prospective risk factors, and hence targets for prevention and treatment.

Despite the variation in prevalence between sites, anaemia made a fairly consistent and substantial independent contribution to disability at the population level. The PAPFs of 5% to 17% (other than in urban Mexico where there was no association) can be compared with the four leading contributors to disability, in terms of median PAPFs, from our earlier analysis in these and other sites; 25·1% for dementia, 11·4% for stroke, 10·5% for limb weakness or paralysis, and 9·9% for arthritis. The contribution of anaemia is similar to that of depression (8·3%) and visual impairment (6·8%), and greater than that of diabetes (4·1%), COPD (3·3%), hearing impairment (2·2%) and ischaemic heart disease (0·8%) (Sousa *et al*, 2009). While reverse causality (disability leading

to anaemia rather than *vice versa*) cannot be completely excluded, most of the other chronic disease contributors to disability were included in the multivariate model. However, the impact of anaemia is best studied using longitudinal data, and we will use our recently completed incidence wave data, a follow-up of all participants 3–5 years after baseline assessment (Ferri *et al*, 2012; Prince *et al*, 2012) to establish the contribution of baseline anaemia to incident dementia, cognitive decline, dependence and mortality. This may help to settle the question of the threshold at which low haemoglobin, in these populations, should be considered to be of clinical significance. The literature is inconsistent on this point. In USA NHANES III the haemoglobin threshold below which mortality rose significantly was 10 g/l lower in non-Hispanic blacks than in non-Hispanic whites and Mexican Americans (Patel *et al*, 2009). However, no such interaction with ethnicity was observed in North Carolina (Denny *et al*, 2006). Findings from the Cardiovascular Health Study suggest that a higher haemoglobin threshold than that applied by the WHO may identify more people at equivalently raised mortality risk (Zakai *et al*, 2005).

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## Authorship contributions and conflicts of interest

The authors worked collectively to develop the protocols and methods described in this paper. Martin Prince led the research group and Cleusa Ferri acted as research coordinator. Juan Llibre Rodriguez (Cuba), Daisy Acosta (Dominican Republic), Aquiles Salas (Venezuela), Ana Luisa Sosa (Mexico) were principal investigators responsible for the field work in their respective countries. Beatriz Marcheco Teruel led the genetics work in Cuba and she and Paul McKeigue led the admixture component. Martin Prince and Renata Bryce conducted the analyses and prepared the first draft of this paper. Other authors reviewed the manuscript, provided further contributions and suggestions. All authors read and approved the final manuscript. There are no conflicts of interest.

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