# Consistent ethnic specific differences in diabetes risk and vitamin D status in the National Health and Nutrition Examination Surveys

Monika H.E. Christensen[a,b], Robert K. Scragg[b,*]

[a] Department of Clinical Science, University of Bergen, Bergen, Norway
[b] School of Population Health, University of Auckland, Auckland, New Zealand

ABSTRACT

Previous findings from the Third National Health and Nutrition Examination Survey (NHANES III), a representative sample of the US population carried out in 1988–1994, showed an inverse association between diabetes risk and serum concentrations of 25-hydroxyvitamin D (25(OH)D) in non-Hispanic whites and Mexican-Americans but not in non-Hispanic blacks. The study aim was to determine if this same pattern in ethnic variation occurred in more recent NHANES surveys. Cross-sectional data came from the NHANES carried out from 1988 to 1994 (NHANES III) and from 2001 to 2006 (NHANES 01-06). The analysis included 11,331 people (5641 non-Hispanic white, 2714 non-Hispanic black and 2976 Mexican American) without known diabetes mellitus, fasting for $\geq 8$ h and aged $\geq 20$ years, with available measurements of 25(OH)D, fasting glucose, fasting insulin and body mass index (BMI). Adjusting for age, gender, BMI, leisure time physical activity and season, higher levels of 25(OH)D were associated with decreased fasting glucose, decreased fasting insulin, and decreased diabetes risk in both non-Hispanic whites and Mexican Americans for both surveys and when combined. When combining NHANES III and NHANES 01-06 the odds ratio (95% confidence interval) for having diabetes was 0.28 (0.19, 0.41) in the highest 25(OH)D quartile compared to the lowest quartile in non-Hispanic whites, and 0.13 (0.06, 0.28) in Mexican Americans (both $p < 0.0001$); but 1.54 (0.62, 3.82) in non-Hispanic blacks, among whom 25(OH)D was not associated with fasting glucose, fasting insulin, or diabetes risk ($p > 0.05$). There was a significant interaction between non-Hispanic whites and Mexican Americans combined, compared with non-Hispanic blacks, when 25(OH)D was regressed against fasting glucose ($p = 0.016$) but not against fasting insulin ($p > 0.05$).

The major finding in both NHANES surveys of consistent inverse associations between serum 25(OH)D concentrations and diabetes risk in non-Hispanic whites and Mexican Americans, but not in non-Hispanic blacks, suggests this finding is unlikely due to chance.

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* Corresponding author at: School of Public Health, University of Auckland, Private Bag 92019, Auckland Mail Centre, 1142, New Zealand.
E-mail address: r.scragg@auckland.ac.nz (R.K. Scragg).

## 1. Introduction

Low blood concentrations of 25-hydroxyvitamin D (25(OH)D) have been associated with several chronic diseases, including type 2 diabetes mellitus [1,2]. An association between low 25(OH)D levels and poor glycaemic control has been reported in previous studies [3–6]. The mechanisms for how vitamin D influences glucose tolerance are not fully understood. Low 25(OH)D levels have been associated with reduced β-cell function and increased insulin resistance [7], mechanisms that possibly explain how vitamin D might influence glucose control.

Only a few epidemiological studies have investigated ethnic specific differences in the association between vitamin D status and glucose control. As non-Hispanic blacks have increased risk of diabetes mellitus and lower circulating 25(OH)D levels, compared with non-Hispanic whites, a connection between low 25(OH)D levels and glycaemia is plausible [8,9]. Despite this, our group has previously, based on the National Health and Nutrition Examination survey (NHANES) III data, reported that serum 25(OH)D is inversely associated with diabetes in non-Hispanic whites and Mexican Americans, but not in non-Hispanic blacks [3]. However, this study also showed that non-Hispanic blacks had lower 25(OH)D levels and higher prevalence of undiagnosed diabetes compared to non-Hispanic whites. Additionally, a smaller study of obese children and adolescents showed an inverse correlation between HbA1c and vitamin D status in Caucasians, and a trend towards significance in Hispanics but no correlation in African Americans [10], confirming an ethnic specific association between diabetes risk and vitamin D status.

It is possible our earlier finding of an ethnic variation in the association between serum 25(OH)D concentration and diabetes risk from NHANES III was due to chance. In this paper, we have included data from both NHANES III and NHANES 01-06 surveys to determine if ethnic variation in the association between vitamin D status and diabetes risk is consistent in both surveys. Further, combining both NHANES survey periods enhances the number of participants, and increases the statistical power to analyze the relationship that circulating 25(OH)D concentration has with fasting glucose, fasting insulin and diabetes risk in the main U.S. ethnic groups surveyed in NHANES (non-Hispanic whites, non-Hispanic blacks and Mexican Americans).

## 2. Material and methods

### 2.1. Survey design

The data reported in this paper come from NHANES collected from 1988 to 1994 (NHANES III), and the surveys collected two-yearly from 2001 to 2006 (NHANES 01-06). These cross-sectional surveys were carried out by the National Center for Health Statistics of the Center for Disease Control and Prevention and are representative for the US civilian non-institutionalized population at the time of each survey. A stratified, multistage sampling design was used to recruit participants from household clusters, with oversampling of non-Hispanic blacks and Mexican Americans. Full details have been published of all survey methods, including sampling, interviews at home, examinations at mobile centres, laboratory measurements, ethical approval, and informed consents [11,12].

### 2.2. Data collection

Information on a wide range of variables, such as age, gender, race/ethnicity (self-assigned as non-Hispanic white, non-Hispanic black, Mexican American or other) was collected at the first interview of the participants, carried out at their homes. Physical examination was conducted within two months of the home interview at mobile examination centre. Weight was measured in pounds (and later converted to kilograms) on electronic scales with participants dressed in underpants, disposable light clothing and slippers. Height was measured to the nearest millimetre while standing with a fixed vertical backboard. Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters. Leisure time physical activity was self-reported and participants were asked if they had undertaken a range of common physical activities in the last month. Metabolic equivalents were assigned for each activity. In participants aged ≥60 years moderate and vigorous activity was classified as any activity with metabolic equivalent ≥3.0 or ≥6.0, respectively, whereas in participants aged 20–59 years the metabolic equivalent for moderate and vigorous activity was ≥3.5 or ≥7.0, respectively [13]. Past history of diabetes mellitus was defined if doctors had ever told the participants that they had diabetes or if they were currently taking diabetes medications. Participants without a medical diagnosed diabetes at inclusion were classified as having diabetes if their fasting morning glucose level was ≥7.0 mmol/L [14].

### 2.3. Blood tests

Blood samples collected during the examination were centrifuged, frozen on site and stored at $-70\,^{\circ}C$ until analysed. A radioimmunoassay kit (DiaSorin, Inc., Stillwater, Minnesota) was used for measuring serum 25(OH)D. Analyses were conducted at the National Center for Environmental Health, CDC, Atlanta, GA. Reformulation of the 25(OH)D DiaSorin kit caused an assay drift, resulting in higher weighted mean concentrations of 25(OH)D in the time-period 1988–1994 compared to 2001–2006. The following equation was used to adjust for this drift: NHANES III 25(OH)$D_{2000-2006RIAassay} = (0.8429*$NHANES III 25(OH)D (nmol/L) $_{1988-1994RIAassay}) + 2.5762$ [15]. The adjusted 25(OH)D data files posted in November 2010 were also used for 2003–2004 and 2005–2006 to correct for assay drift from 2001 to 2002 [15]. Plasma glucose was measured by a modified Hexokinase enzymatic method in all surveys; while plasma insulin was measured by a radioimmunoassay in NHANES III and NHANES 01-02, an immunoenzymometric method in NHANES 03-04 and an ELISA method in NHANES 05-06.

### 2.4. Survey participants

A total of 17,030 adults, ≥20 years, participated in the NHANES survey from 1988 to 1994, while 14,531 participants were included from 2001 to 2006. Data in this report are restricted to 11,331 non-