BMJ Open

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Journal:	*BMJ Open*
Manuscript ID	bmjopen-2016-015214
Article Type:	Research
Date Submitted by the Author:	21-Nov-2016
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Primary Subject Heading:	Public health
Secondary Subject Heading:	Global health, Diabetes and endocrinology, Epidemiology
Keywords:	PUBLIC HEALTH, General diabetes < DIABETES & ENDOCRINOLOGY, EPIDEMIOLOGY

Household and familial resemblance in risk factors for type 2 diabetes and related cardio-metabolic diseases in rural Uganda

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Word count: 3068

ABSTRACT (269 words)

OBJECTIVES

Prevention of type 2 diabetes (T2D) has been successfully established in randomized clinical trials. However, the best methods for the translation of this evidence into effective population-wide interventions remain unclear. To assess whether households could be a target for T2D prevention and screening, we investigated the resemblance of T2D risk factors at household level and by type of familial dyadic relationship in a rural Ugandan community.

METHODS

This cross-sectional household based study included 437 individuals ≥13 years of age from 90 rural households in south-western Uganda. Resemblance in HbA1c, anthropometry, blood pressure, fitness status and sitting time were analysed using a general mixed model with random effects (by household or dyad) to calculate household intraclass-correlation coefficients (ICC) and dyadic regression coefficients. Logistic regression with household as a random effect was used to calculate the odd ratios (ORs) for individuals having a condition or risk factor if another household member had the same condition.

RESULTS

The strongest degree of household member resemblances in T2D risk factors was seen in relation to fitness status (ICC=0.24), HbA1c (ICC=0.18), and systolic blood pressure (ICC=0.11). Regarding dyadic resemblance, the highest standardised regression coefficient was seen in fitness status for spouses (0.54 95%CI:0.32;0.76), parent-offspring (0.41 95%CI:0.28;0.54) and siblings (0.41 95%CI:0.25;0.57). Overall, parent-offspring and sibling pairs were the dyads with strongest resemblance, followed by spouses.

CONCLUSIONS

The marked degree of resemblance in T2D risk factors at household level and between spouses, parent-offspring, and sibling dyads suggest that shared behavioural and environmental factors may influence risk factor levels among cohabiting individuals, which point out the potential of the household setting for screening and prevention of T2D.

STRENGHT AND LIMITATIONS OF THIS STUDY

- The household based approach visiting the families in the home setting resulted in a high individual response rate (97.5%) and thus only minimal risk of selection bias in dyad representativeness.
- The study included a comprehensive set of risk factor measurements and several types of dyadic relationships, which enabled us to investigate resemblance in multiple risk factors for type 2 diabetes in genetic and non-genetic relationships and across generations.
- The cross-sectional design prevents us from concluding on whether the spousal resemblance was due to shared risk behaviours or assortative mating, and for the genetic relationships we cannot distinguish between shared genes and shared environment/behaviours.
- The size of the intraclass-correlation coefficients should only be interpreted as a tool to investigate which risk factors resemble most strongly at the household level in the present cohort, and should be directly compared to other cohorts.

INTRODUCTION

Globally the number of people with diabetes is increasing rapidly, and in Sub-Saharan African (SSA) countries like Uganda the numbers will more than double within the next two decades.[1] The current state-of-the-art for prevention of type 2 diabetes (T2D) in high-risk individuals, consisting of a healthy diet, increased physical activity and weight loss, has been successfully established in randomized controlled trials from both high-income[2] and middle-income countries.[3] However, the best methods for the translation of clinical proof-of-concept evidence of prevention into low-cost effective and feasible population-wide interventions remains unclear in high-income countries, and especially low- and middle-income countries.

In settings where daily life is focused around the family, households may present an opportunity to target several individuals simultaneously. Most of the variation in the risk of T2D in high-income countries is explained by lifestyle and behavioural factors, or by the interaction of lifestyle behaviours with genetic factors,[4;5] and household members are likely to share lifestyle behaviours and to some extent genes. Shared daily environment may partly explain the observed resemblance between household members such as spouses in risk factors related to the development of T2D like obesity,[6;7] exercise levels,[8;9] raised blood pressure[7;9;10] and smoking.[9;10] Further, spouses of a person with T2D have been shown to have higher fasting plasma glucose[11;12] and higher risk of developing T2D as compared to individuals with no spousal history of T2D.[12;13] For familial relations that include a genetic relationship the degree of diabetes risk concordance[13] and resemblance in obesity,[14] glycaemic levels,[15] blood pressure levels[16] and aerobic fitness status[17] are consistently higher than for spouses or adoptees, likely due to a combination of genetic and shared environmental effects.

In SSA a family or a household often consists of multiple members and types of relationships (dyads). Yet, little is known about T2D risk factor resemblance among individuals sharing daily life in a low-income country in epidemiological transition. Therefore, the ojective of this study was to investigate resemblance of T2D risk factors at household level and by type of familial dyadic relationship in a rural Ugandan community.

METHODS

Study design and setting

This cross-sectional study was part of a larger study examining households with and without a member with previously diagnosed T2D.[18] Data were collected between December 2012 and March 2013 in Kasese District, Uganda. The area is mountainous and the majority of the inhabitants are peasants and live in houses made of mud or unburned bricks with iron sheet roofs. Average household size is 5.3 individuals.[19] One hundred households were approached and ninety agreed to participate. Reasons for non-participation were lack of time. Of the 90 households, half included a person diagnosed with T2D, selected from diabetes patient records at the nearby hospital diabetes clinic. Households without diagnosed T2D were selected using a random sampling plan.[18] To be included in the study, the household should consist of at least two generations, have at least three individuals aged ≥13 years, and no member with diagnosed HIV/AIDS, type 1 diabetes, or active tuberculosis. Households were defined as people living together and sharing food on a daily basis. All members aged 13 years or above, who had lived in the household for more than three months prior to the visit by the survey team were invited to participate (response rate 97.5%). Details of sampling, inclusion and exclusion criteria are described elsewhere.[18]

Ethics

Prior to data collection, the households were visited, the overall aim of the project was verbally explained and an information leaflet was handed out. On the day of data collection, verbal information about the project was given again and the participants were given time to ask questions. Verbal and written consent was obtained from all participants who still agreed to participate. For participants below 18 years of age, a written consent from a caretaker was obtained from the caretaker. The study was approved by the Uganda National Council of Science and Technology (ADM 154/212/01), Makerere University School of Medicine Research & Ethics Committee (REC-REF 2012-183), St.Francis Hospital Nsambya, and Kagando Hospital.

Procedures

After the initial presentation of the study, a household profile was developed, detailing family structure, members, dyads (relationship between every pair of members) and age. Dwelling elevation (meters above sea-level, MSL) was measured using a Garmin Trex10 (Garmin, UK).

HbA1c (%) was measured using an Afinion AS100 Analyzer (Axis Shield PoC, Norway) and values were converted to mmol/mol.[20] Diabetes was defined as HbA1c≥48 mmol/mol and HbA1c levels between 42-47 mmol/mol was defined as dysglycaemia.[21] Blood pressure was measured three times in sitting position after at least 10 minutes of rest (Omron M6 HEM7211E, Kyoto, Japan). Hypertension was defined as a systolic blood pressure≥140 mm Hg, or a diastolic blood pressure≥90 mm Hg,[22] averaged over the last two blood pressure readings. Body weight measured using a flat scale (model 876, SECA, UK) and height measured using a portable stadiometer (Model 213, SECA UK) were used to calculate body mass index (BMI) as weight(kg)/height(m)^2. Underweight, normal weight, overweight and obesity were defined according to the World Health Organization (WHO) classifications for adults[23] and for adolescents aged from 13 to 19 years according to WHO Child Growth Standards.[24] For dyads where one member could be below 19 years of age (parent-offspring, siblings and grandparent-grandchild) a Z-score of height-for-age was calculated and used instead of height (cm) for both dyad members. The Z-score was calculated according to de Onis et al. (2007) and individuals ≥19 years of age were handled as the oldest category in the standards WHO Child Growth Reference.[24]

As a measure of aerobic fitness status, an eight-minute step test was conducted to estimate aerobic capacity (maximal oxygen uptake, VO_2-max [mlO_2/min/kg body weight]) and managed according to the Cambridge Protocol.[25] Fifty individuals did not perform/complete at least four minutes of the step test. In data analyses using fitness status as a continuous variable, these individuals were excluded, whereas in data analyses where fitness status was used as a dichotomous variable, the 50 individuals were coded as unfit with the exception of those who had recently given birth or had an acute illness (n=5).

Household socio-economic status (SES), and individual educational level, age, sex, disease status and smoking were assessed using questionnaires.[18] Daily sitting time was assessed using a locally adapted version of the International Physical Activity Questionnaire (IPAQ).[26]

Statistical analysis

The amount of resemblance in T2D risk factors in individuals living within the same household was assessed calculating intraclass-correlation coefficients (ICC) with general mixed models with household as a random effect, adjusting for sex, age, SES and household size.

Dyadic relationships were restricted to spouses, parent-offspring, grandparent-grandchild and sibling dyads and analysed as distinguishable members based on sex for spousal dyads (husband dyad number one and wife dyad number two), birth order for sibling dyads (oldest sibling dyad number 1) and age for parent-offspring and grandparent-grandchild dyads (parent and grandparents as dyad number 1 respectively).[27] As non-independence was assumed, a mixed model was used to analyse the dyadic resemblance between the same risk factor in the two dyad members. Our primary analyses modelled the risk factors HbA1c, blood pressure, height, BMI, fitness status and sitting time, separately, in dyad member 2 as a function of the same risk factor in dyad member 1. Random effects were dyad member 1 (to account e.g. for a parent having more than one child) or household (to account for more than one of the same type of dyad occurring per household). For dyadic relationships regression coefficient estimates were reported with 95% confidence intervals. Logistic regression with household as a random effect was used to calculate the odd ratio (OR) of an individual having a condition if someone else in the household had the same condition. ORs are reported with 95% confidence intervals. Explanatory variables were introduced sequentially: individual level (sex, age); dyad level (age-difference between the dyad members); and household level (socio-economic status, elevation of the dwelling, household size). Statistical significance was set as $p<0.05$.

For analyses including HbA1c, individuals with diagnosed T2D (n=45) were excluded and for analyses including blood pressure measures individuals with diagnosed hypertension (n=32) were excluded. All statistical analyses were performed using Stata 14.1 SE (StataCorp LP USA).

RESULTS

From the 90 households we identified a total of 947 dyads of which 91 (9.6%) were spouses, 283 (29.8%) were parent-offspring dyads, 97 (10.2%) were grandparent-grandchild dyads and 148 (15.6%) were sibling dyads. The remaining 330 dyads were primarily in-laws and uncle/aunt-nephew/niece dyads (not included in this analysis). General characteristics and cardio-metabolic risk factors at household level and by dyadic relationship are summarized in Table 1. In 84 (93.3%) households all meals were eaten within the household. Median dwelling elevation was 1,177 meters above sea-level (MSL) (range 951-1,742 MSL).

Table 1. General characteristics and cardio-metabolic risk factors at household level and by dyadic relationships

(n)	Households (90)	Dyads by type (n)											
		Spouses (91)		Parent-offspring (283)				Grandparent-grandchild (97)				Siblings (148)	
Members (n unique)		Wives (91)	Husbands (89)	Parent (150)		Offspring (164)		Grandparent (64)		Grandchild (64)		Sisters (79)	Brothers (71)
				Mothers (88)	*Fathers (62)*	*Daughters 81*	*Sons (83)*	*Grandmothers (41)*	*Grandfathers (23)*	*Granddaughters (25)*	*Grandsons (39)*		
Individuals in household	5 (range 3-10)												
Age (Years)*	38.7 [33.0;43.1]	51.0 [42.7;57.4]	56.1 [49.6;67.4]	53.7 [47.6;63.1]	60.4 [52.6;68.4]	21.3 [15.8;30.7]	19.7 [16.0;26.7]	67.5 [56.6;72.7]	68.4 [60.5;74.7]	16.8 [13.8;18.8]	16.8 [14.6;19.5]	21.5 [15.4;39.6]	19.0 [16.5;24.0]
Age-difference (years)*[1]	46.0 [38.7;54.0]	6.1 [3.0;11.0]		32.6 [27.0;38.2]				50.2 [41.7;56.0]				4.8 [3.0;8.0]	
Diagnosed T2D n (%)	45 (50)	9 (9.9)	29 (32.6)	12 (13.6)	23 (37.1)	2 (2.5)	1 (1.2)	8 (19.5)	6 (26.1)	0 (0)	0 (0)	3 (3.8)	1 (1.4)
Undiagnosed diabetes or dysglycaemia n (%)	22 (24.4)	12(13.2)	5 (5.6)	11 (12.5)	4 (6.5)	5 (6.2)	1 (1.2)	6 (14.6)	2 (8.7)	1 (4.0)	0 (0)	8 (10.1)	1 (1.4)
Diagnosed Hypertension n (%)	28 (31.1)	10 (11.0)	14 (15.7)	12 (13.6)	10 (16.1)	0 (0)	0 (0)	12 (29.3)	6 (26.1)	0 (0)	0 (0)	2 (2.5)	1 (1.4)
Undiagnosed Hypertension n (%)	67 (74.4)	16 (17.6)	23 (26.1)	17 (19.5)	20 (32.8)	3 (3.7)	3 (3.6)	8 (19.5)	10 (45.5)	0 (0)	0 (0)	3 (3.9)	1 (1.4)
HbA1c (mmol/mol)[2]	35.4 (3.2)	36.9 (5.5)	35.8 (5.9)	37.3 (5.5)	36.4 (6.5)	35.0 (4.4)	34.6 (5.7)	38.3 (4.9)	38.0 (8.7)	35.9 (3.0)	34.4 (3.8)	36.0 (5.3)	34.4 (4.2)
Systolic blood pressure (mmHg)*[3]	128 [123;137]	134 [117;149]	139 [127;164]	137 [118;155]	151 [132;170]	118 [112;129]	124 [117;131]	152 [134;167]	164 [153;192]	117 [112;125]	125 [114;131]	120 [113;131]	122 [117;130]
Diastolic blood pressure (mmHg)*[3]	78 [74;82]	80 [74;89]	84 [76;92]	84 [79;91]	87 [79;95]	75 [71;81]	72 [69;80]	86 [73;91]	91 [79;94]	73 [66;78]	73 [66;78]	75 [70;81]	72 [66;78]
Height (cm)	155.2 (3.8)	152.4 (5.4)	161.3 (5.3)	151.5 (5.1)	160.6 (5.3)	153.5 (6.6)	158.4 (8.4)	150.4 (5.2)	159.0 (4.5)	153.3 (6.7)	156.3 (10.1)	152.7 (6.2)	160.3 (7.7)
Short stature n (%)[4,5]	78 (86.7)	30 (32.8)	49 (55.7)	33 (37.5)	38 (61.3)	19 (23.5)	45 (54.2)	22 (53.7)	15 (68.2)	3 (12.0)	20 (52.3)	19 (24.1)	35 (49.3)
Body mass index*[5]	21.7 [20.7;23.2]	23.1 [21.0;25.3]	21.5 [19.6;25.0]	22.4 [19.7;24.6]	22.1 [19.6;25.4]	22.4 [20.2;24.4]	20.4 [19.0;21.5]	21.2 [18.3;24.7]	21.0 [19.3;25.0]	20.8 [18.6;23.7]	19.9 [18.3;21.2]	22.4 [19.8;24.8]	19.2 [19.2;21.6]
Underweight n (%)	27 (30.0)	9 (9.9)	8 (9.1)	13 (14.8)	6 (9.7)	5 (6.2)	2 (2.4)	11 (26.8)	3 (13.6)	1 (4.0)	1 (2.6)	4 (5.1)	1 (1.4)
Overweight n (%)	52 (57.8)	25 (27.5)	24 (27.3)	19 (21.6)	20 (32.3)	19 (23.5)	5 (6.0)	10 (24.4)	6 (27.3)	4 (16.0)	0	21 (26.6)	2 (2.8)
Fitness status (VO2-max: ml O_2/min/kg)[6]	38.5 (4.7)	34.3 (6.8)	33.5 (8.8)	32.0 (6.7)	32.7 (7.2)	37.3 (6.6)	44.6 (6.8)	29.1 (6.8)	29.2 (6.0)	38.9 (5.9)	46.0 (4.6)	37.0 (7.0)	44.8 (5.9)
Unfit n (%)[7]	72 (80.0)	35 (40.2)	39 (44.3)	43 (49.4)	25 (41.0)	24 (29.6)	30 (36.1)	30 (75.0)	14 (63.6)	5 (20.0)	15 (39.5)	26 (32.9)	25 (35.2)
Sitting per day (min)*	275.4 [225;310]	208 [169;279]	274 [189;351]	231 [189;334]	283 [197;373]	261 [204;326]	240 [189;369]	274 [197;380]	257 [189;343]	274 [180;334]	240 [159;360]	257 [204;326]	238 [180;354]
Smoking status n (%)													
Never smoked	52 (57.8)	71 (78.0)	59 (66.3)	57 (64.8)	39 (62.9)	77 (95.1)	68 (81.9)	22 (53.7)	13 (56.5)	24 (96.0)	38 (97.4)	70 (88.6)	59 (83.1)
Former smoker	38 (42.2)	11 (12.1)	21 (23.6)	19 (21.6)	17 (27.4)	2 (2.5)	9 (10.8)	13 (31.7)	6 (26.1)	0 (0)	0 (0)	5 (6.3)	6 (8.5)
Current smoker	21 (23.3)	9 (9.9)	9 (10.1)	12 (13.6)	6 (9.7)	2 (2.5)	6 (7.2)	6 (14.6)	4 (17.4)	1 (4.0)	1 (2. 6)	4 (5.1)	6 (8.5)
Years of education*	5.3 (2.2)	2 [0;6]	6 [3;7]	2 [0;4)	5 [1;7]	6 [5;10]	7 [5;10]	0 [0;2]	5 [1;6]	6 [5;7]	6 [4;8]	6 [3:9]	7 [5;10]

Data are presented as mean (SD); *Median [p25;p75]]; 1: At household level age-difference is between the oldest and youngest individual in the household. 2: Individuals with diagnosed diabetes are excluded; 3: Individuals with diagnosed hypertension are excluded. 4: Short stature is defined as age (months) z-score below -2SD or final height for males below 161.9cm and for females below 150.1cm [24]; 5: missing value on 1 man; 6: 50 individuals did not complete the steptest. 7: Data missing on six individuals because of pregnancy, recent delivery, sickness, or technical error.

Household resemblance in T2D risk factors

At household level ICCs showed statistically significant household member resemblance for four risk factors; After adjustment for age and sex ICCs were statistically significant for fitness status (ICC=0.24, p<0.001), HbA1c (ICC=0.18, p<0.001), BMI (ICC=0.08, p=0.010) and systolic blood pressure (ICC=0.11, p=0.003), while only a tendency was observed for diastolic blood pressure (ICC=0.06, p=0.06). Additional adjustment for SES, household size or dwelling elevation did not change the ICCs.

Dyad resemblance

Dyad resemblance in T2D risk factors is shown as regression coefficients adjusted for age-difference and sex in Table 2. Sibling and parent-offspring dyads both had five statistically associated risk factors with siblings being associated in measures of HbA1c, systolic blood pressure, diastolic blood pressure, height and fitness status and parent-offspring dyads in HbA1c, systolic blood pressure, height, fitness status and sitting time. Spouses were statistically significantly associated in systolic blood pressure and fitness status while grandparent-grandchild dyads were only associated with regard to diastolic blood pressure. None of the four dyad types had a statically significant association for BMI.

Standardized regression coefficients are shown in Table 3. For spouses, parent-offspring and sibling dyads the standardized regression coefficients were highest for fitness status.

Table 2. Dyad regression coefficients for type 2 diabetes risk factors (adjusted for age-difference and sex)

(n)	Spouses (91)	Parent-offspring (283)	Grandparent-grandchild (97)	Siblings (148)
HbA1c (%)[1]	0.18 [-0.09;0.45]	0.16* [0.02;0.29]	0.07 [-0.8;0.22]	0.28* [0.13;0.44]
Systolic Blood Pressure (mmHg)[2]	0.27* [0.01;0.53]	0.10* [0.04;0.16]	0.08 [-0.02;0.19]	0.18* [0.01;0.36]
Diastolic Blood pressure (mmHg)[2]	0.10 [-0.13;0.34]	0.02 [-0.07;0.10]	0.14* [0.02;0.27]	0.16* [0.01;0.32]
Height (cm or SD)[4]	0.07 [-0.13;0.26]	0.35* [0.19;0.52]	0.10 [-0.17;0.38]	0.26* [0.09;0.42]
Body mass index (kg/m^2)	0.19 [-0.04;0.42]	0.02 [-0.07;0.12]	-0.01 [-0.14;0.13]	0.11 [-0.06;0.29]
Fitness status (mlO_2/min/kg)[3]	0.42* [0.25;0.59]	0.46* [0.31;0.60]	-0.08 [-0.37;0.20]	0.38* [0.22;0.53]
Daily sitting time (minutes)	0.09 [-0.05;0.24]	0.15* [0.04;0.27]	0.10 [-0.07;0.27]	0.09 [-0.08;0.27]

Values are presented as regression coefficients [95% conf. interval]; Coefficients express the difference in each risk factor in dyad member 2 per unit difference in that same risk factor in dyad member 1. *p<0.05; [1]Individuals with diagnosed diabetes were excluded; [2]Individuals with diagnosed hypertension were excluded; [3]In 15% of the dyads, one member did not complete the step test; [4]For spouses height (cm) is used while for parent-offspring, grandparent-grandchild and siblings height-for-age is used and not adjusted for age-difference or sex.

Table 3. Standardized regression coefficients for type 2 diabetes risk factors (adjusted for age-difference and sex)

	Spouses (91)	Parent-offspring (283)	Grandparent-grandchild (97)	Siblings (148)
HbA1c[1]	0.19 [-0.11;0.50]	0.21* [0.02;0.40]	0.12 [-0.13;0.37]	0.26* [0.11;0.42]
Systolic Blood Pressure[2]	0.28* [0.01;0.54]	0.20* [0.08;0.33]	0.22 [-0.06;0.50]	0.20* [0.01;0.39]
Diastolic Blood pressure[2]	0.10 [-0.14;0.35]	0.02 [-0.11;0.15]	0.27* [0.03;0.05]	0.20* [0.01;0.39]
Height for age[4]	0.07 [-0.13;0.28]	0.26* [0.14;0.37]	0.08 [-0.13;0.31]	0.26* [0.09;0.42]
Body mass index	0.16 [-0.04;0.37]	0.02 [-0.11;0.16]	0.02 [-0.20;0.24]	0.14 [-0.03;0.31]
VO_2-max[3]	0.54* [0.32;0.76]	0.41* [0.28;0.54]	-0.09 [-0.38; 0.21]	0.41* [0.25;0.57]
Daily sitting time	0.11 [-0.09;0.31]	0.17* [0.04;0.32]	0.11 [-0.09;0.32]	0.09 [-0.10;0.27]

Values are presented as standardized regression coefficients [95% conf. interval]; *p<0.05

Concordance in risk factors

The results of the logistic regression models are shown in Table 4. At household level effect estimates showed that if one member in the household had undiagnosed diabetes or dysglycaemia the OR of another household member having the same status was increased almost 20 times. Having diagnosed hypertension in the household increased the odds of another member having diagnosed or undiagnosed hypertension 2.6 times whereas undiagnosed hypertension increased the odds of diagnosed or undiagnosed hypertension in another member 4.8 times. The ORs of being overweight or obese, underweight, unfit, smoker or former smoker were all statistically significantly higher if another member of the household had the same status as compared to if no one in the household had the same status (Table 4).

Table 4. Odd ratios of having a condition as a function of the disease or risk factor status in other members of the same household (adjusted for age, sex and household size)

Exposure (status	Outcome	Household level
Diagnosed diabetes	*Undiagnosed diabetes or dysglycaemia*	0.8 [0.4; 2.0]
Undiagnosed diabetes or dysglycaemia	*Undiagnosed diabetes or dysglycaemia*	19.8 [11.0; 35.5]*
Diagnosed hypertension	*Diagnosed or undiagnosed hypertension*	2.6 [1.5; 4.5]*
Undiagnosed hypertension	*Diagnosed or undiagnosed hypertension*	4.8 [2.9; 8.0]*
Short stature	*Short stature*	10.9 [6.9; 17.0]*
Overweight or obesity	*Overweight or obesity*	9.0 [6.1; 13.2]*
Underweight	*Underweight*	13.7 [7.1; 26.3]*
Unfit	*Unfit[5]*	11.2 [7.4; 17.1]*

Smoker	*Smoker*	33.7 [15.8; 71.8]*
Former smoker	*Former smoker*	18.9 [9.4; 38.0]*

Values are presented as odd ratios [95% conf. interval]; *p<0.05; [1]Individuals with diagnosed diabetes were excluded; [2]Individuals with diagnosed hypertension were excluded; [3]In 15% of the dyads, one member did not complete the step test; [4]Not adjusted for age-difference; [5]Unfit is defined as a fitness level below middle derived from VO_2-max and grouped according to Astrand (1960).[28]

DISCUSSION

The results of the present study indicate that individuals living in the same household in rural Uganda share risk factors for T2D and cardio-metabolic diseases. We showed that in particular for systolic blood pressure and fitness status the spousal association was at least as strong as the association between siblings or parent-offspring pairs indicating an effect of shared lifestyle behaviours. For other cardio-metabolic risk factors the resemblance was more prominent between siblings and parent-offspring dyads, whereas grandparent-grandchild dyads were less alike.

To our knowledge this is the first study to investigate the resemblance of multiple cardio-metabolic risk factors in household clusters including several generations living and eating together on a daily basis. A German study of aerobic fitness found an ICC of 0.22 in fitness status in nuclear families, but no association when restricting the analyses to spouses.[29] Our findings of dyad resemblance in HbA1c, blood pressure, height and fitness status are in agreement with other epidemiological studies focusing on a single type of dyad[15;16] or a single type of risk factor.[29;30] We are not aware of studies from low-income countries investigating household or dyad resemblance in risk factors for T2D.

Among the measured risk factors, fitness status had the highest ICC at household level and standardised regression coefficient among spouse, parent-offspring and sibling dyads. The high resemblance in fitness status is partly explained by the high heritability of VO_2-max.[17] However, in contrast to the German study[29] we also found a high association in spousal fitness status suggesting that also shared physical activity patterns may contribute to the high fitness status resemblance in our study population. In the Ugandan situation most often a peasant's wife is also a peasant and offspring help cultivating the family land. Shared daily activities as the explanation for spousal resemblance in fitness status is supported by a French study finding that spouses' physical activity patterns were only similar during weekend days.[31] In addition, for most

of the study participants walking was the primary means of transportation, giving all individuals in the same household the same walking distance and elevation differential when going to e.g. the nearest trading centre. However, adjusting for elevation only gave a modest attenuation of the household ICC or the dyad resemblance in fitness status.

In line with the results of a meta-analysis,[32] spouses resembled each other with regard to systolic blood pressure. Contradicting other studies[6;32] we did not find a statistically significant spousal association for BMI, diastolic blood pressure or HbA1c. Discordance in ethnicity of spouses, low numbers of people living in the household and higher SES have previously been shown to attenuate the spousal association in BMI.[6] However, none of these factors were present or affected the absence of a spousal BMI association on our study. Assortative mating and/or convergence over time are often used to explain spousal resemblance in risk factors for T2D.[8;33] However, studies of assortative mating and risk factors for T2D are almost exclusively from high-income settings,[8;33] and preferences for choice of spouse may differ across geographical, social and ethnic settings. For instance, overweight has traditionally been viewed as a desirable feature in SSA settings[34] whereas it is more stigmatizing in high-income settings.[35] Further, until recently the prevalence of obesity in SSA was low, and results from a Danish study showed a tendency to an increase in assorted marriages between obese spouses along with the obesity epidemic[33]

In contrast to other studies of genetically related individuals, we did not find a relationship in BMI for parent-offspring[14;36] or sibling dyads.[15;30;37] Concerning parent-offspring, a study from the U.S including children from 2-16 years of age suggested that pubertal children are less likely to resemble their parents in BMI than pre-puberty children as children with age grow more independent from parents' behaviours in terms of eating and exercise,[36] which could explain the lack of parent-offspring relationship in our study where some of the parent-offspring dyads included adult offspring. However, stratifying parent-offspring dyads into adolescents and adult offspring or above/below median age-difference did not change the lack of statistical associations. In terms of siblings, another study found sibling dyads to resemble in BMI,[15] but that the sibling BMI correlations were less pronounced during adolescence,[30] decreased with increasing age difference[15] and was higher among home living adolescents than adult siblings living apart.[37] The mean

sibling age difference (7 years) in our study was not markedly different from the mentioned studies, and the siblings lived together. Thus these factors cannot entirely explain the lack of relationship. The last relationship with a genetic component examined in the present study was grandparent-grandchild dyads. Again no relationship was seen in BMI, which is supported by data from a Korean population,[38] but in contrast to a study from Belgium finding a direct association in obesity measures through three generations.[39] Neither the Korean nor the Belgian study reported that grandparents and grandchildren lived together, which they did in our study and could have increased the chance of resemblance in BMI. However, Uganda is a country in transition both in terms of disease burden and nutrition. In addition the Ruwenzori Mountain region was centre of civil strife with a civil war in 1962-1982 and again from 1996-2002, making it likely that grandparents and grandchildren were exposed to very different intrauterine environments and growing up conditions. This hypothesis is supported by the findings of a statistically significant height increment between each of the three generations in our cohort (data not shown), which was not reported in the study from Korea including three generations.[38] Potential unmeasured confounders for BMI may have been unreported/undiagnosed infectious disease such as tuberculosis or HIV/AIDS; both have a fairly high prevalence in the study setting[40] and both affect body weight.

The high ORs in smoking status may partly be explained by a low overall smoking prevalence (7.6%). Further, 63% of the smokers lived together with a least one other smoker. The high resemblance in smoking status is supported by results of a studies finding a high spousal resemblance in smoking status[8] and that both smoking and quitting of smoking spreads in social ties in social networks.[41]

Strengths and limitations

One of the main strengths of this study is the household based approach visiting the families in the home setting resulting in a high individual response rate (97.5%) and thus only minimal risk of selection bias in dyad representativeness. The cross-sectional design prevents us from concluding on whether the spousal resemblance was due to shared risk behaviours or assortative mating, and for the genetic relationships we cannot distinguish between shared genes and shared environment/behaviours. The ICCs reflect the proportion of variances, whereby the sizes of the ICCs cannot be compared to other cohorts or settings.

Thus, the size of ICCs should only be interpreted as a tool to investigate which risk factors resemble most strongly at the household level in the present cohort. Due to the initial sampling of this study population, 50% of the households had a member with diagnosed T2D. We have previously shown that having diagnosed T2D in the household may have positive spill-over effects on the other members[18] potentially due to changes in diet and physical activity due to the diabetes status.[42] This could explain the difference between diagnosed T2D and unknown diabetes/dysglycaemia in the household as a risk factor for unknown diabetes/dysglycaemia in other members of the household.

CONCLUSION

The moderate to strong correlations in T2D risk factors at household level and between spouses, parent-offspring, and sibling dyads suggest that shared behavioural and environmental factors such as physical activity may influence the risk factor level among cohabiting individuals. The marked degree of household resemblance for certain T2D risk factors highlights the potential of the household setting for screening and prevention of T2D. Thus, when one household member presents with elevated glucose, blood pressure, or physical inactivity the entire household could benefit from lifestyle interventions.

Acknowledgement

We thank the people who opened their homes and took time to participate in this study, the field assistants for collecting data and carrying equipment up the mountain slopes, and the Kagando Hospital staff members for their hospitality and support. We also thank Dr. Adam Hulman, Department of Public Health, University of Aarhus, for help with data management; and Soren Brage, University of Cambridge, for assistance with step-test data.

Author contribution statement

Dr. Jannie Nielsen developed the study protocol; collected the data; performed the statistically analyses and the interpretation of data; and drafted, revised and finalized the article.

Dr. Silver K. Bahendeka contributed to the protocol with substantially knowledge concerning diabetes in Uganda and specifically in Kasese district; took part in the later stage and final interpretation of data, and, participated in developing, revising and finalizing the manuscript.

Professor Susan R. Whyte contributed to the development of the study protocol; took part in the later stage and final interpretation of data; and participated in developing, revising and finalizing the manuscript.

Associate Professor Dan W. Meyrowitsch contributed to the development of the study protocol; took part in the later stage and final interpretation of data; and participated in developing, revising and finalizing the manuscript.

Professor Ib C. Bygbjerg contributed to the development of the study protocol; took part in the later stage and final interpretation of data; and participated in developing, revising and finalizing the manuscript.

Professor Daniel R. Witte performed the statistically analysis and the interpretation of data, participated in developing, revising and finalizing the manuscript.

Competing interests

Dr. Nielsen's PhD fellowship was partly funded by Novo Nordisk Fonden (grant no. 29847).

Funding

The study was sponsored by University of Copenhagen, Thorvald Madsens Fond, Aase and Ejnar Danielsens Fond, and Christian and Otilia Brorsons Rejselegat. No sponsor had any influence on the study design; data collection, analysis, or interpretation; or the writing of this article. The remaining authors have declared no conflict of interest.

Data sharing statement

No additional data available.

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STROBE CHECKLIST

Study: Household and familial resemblance in risk factors for type 2 diabetes and related cardio-metabolic diseases in rural Uganda

Type of study: Cross-sectional

	Item No	Recommendation	Page
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/ rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	5
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*6*
Bias	9	Describe any efforts to address potential sources of bias	5
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7
		(*b*) Describe any methods used to examine subgroups and interactions	7
		(*c*) Explain how missing data were addressed	6
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	9
		(b) Give reasons for non-participation at each stage	9
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8+9
		(b) Indicate number of participants with missing data for each variable of interest	9
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	10+11
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10+11
		(*b*) Report category boundaries when continuous variables were categorized	9
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	11
Discussion			
Key results	18	Summarise key results with reference to study objectives	12
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	13
Generalisability	21	Discuss the generalisability (external validity) of the study results	14+15
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	16

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Household and familial resemblance in risk factors for type 2 diabetes and related cardio-metabolic diseases in rural Uganda: A cross-sectional community sample

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2016-015214.R1
Article Type:	Research
Date Submitted by the Author:	27-Jun-2017
Complete List of Authors:	Nielsen, Jannie ; University of Copenhagen, Global Health Section, Department of Public Health Bahendeka, Silver; St. Francis Hospital Nsambya, Whyte, Susan; University of Copenhagen, Department of Anthropology Meyrowitsch, Dan; University of Copenhagen, Global Health Section, Department of Public Health Bygbjerg, Ib; University of Copenhagen, Global Health Section, Department of Public Health Witte, Daniel; University of Aarhus, Department of Public Health; Danish Diabetes Academy
Primary Subject Heading:	Public health
Secondary Subject Heading:	Global health, Diabetes and endocrinology, Epidemiology
Keywords:	PUBLIC HEALTH, General diabetes < DIABETES & ENDOCRINOLOGY, EPIDEMIOLOGY

Household and familial resemblance in risk factors for type 2 diabetes and related cardio-metabolic diseases in rural Uganda: A cross-sectional community sample

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Word count: 3304

ABSTRACT

OBJECTIVES

Prevention of type 2 diabetes (T2D) has been successfully established in randomized clinical trials. However, the best methods for the translation of this evidence into effective population-wide interventions remain unclear. To assess whether households could be a target for T2D prevention and screening, we investigated the resemblance of T2D risk factors at household level and by type of familial dyadic relationship in a rural Ugandan community.

METHODS

This cross-sectional household based study included 437 individuals ≥13 years of age from 90 rural households in south-western Uganda. Resemblance in HbA1c, anthropometry, blood pressure, fitness status and sitting time were analysed using a general mixed model with random effects (by household or dyad) to calculate household intraclass-correlation coefficients (ICC) and dyadic regression coefficients. Logistic regression with household as a random effect was used to calculate the odds ratios (ORs) for individuals having a condition or risk factor if another household member had the same condition.

RESULTS

The strongest degree of household member resemblances in T2D risk factors was seen in relation to fitness status (ICC=0.24), HbA1c (ICC=0.18), and systolic blood pressure (ICC=0.11). Regarding dyadic resemblance, the highest standardised regression coefficient was seen in fitness status for spouses (0.54 95%CI:0.32;0.76), parent-offspring (0.41 95%CI:0.28;0.54) and siblings (0.41 95%CI:0.25;0.57). Overall, parent-offspring and sibling pairs were the dyads with strongest resemblance, followed by spouses.

CONCLUSIONS

The marked degree of resemblance in T2D risk factors at household level and between spouses, parent-offspring, and sibling dyads suggest that shared behavioural and environmental factors may influence risk factor levels among cohabiting individuals, which point to the potential of the household setting for screening and prevention of T2D.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- The household-based approach, which involved visiting the families in the home setting, resulted in a high individual response rate (97.5%) and thus only minimal risk of selection bias in dyad representativeness.
- The study included a comprehensive set of risk factor measurements and four types of dyadic relationships, which enabled us to investigate resemblance in multiple risk factors for type 2 diabetes in genetic and non-genetic relationships and across generations.
- The cross-sectional design prevents us from concluding on whether the spousal resemblance was due to shared risk behaviours or assortative mating, and for the genetic relationships we cannot distinguish between shared genes and shared environment/behaviours.
- The size of the intraclass-correlation coefficients should only be interpreted as a tool to investigate which risk factors resemble most strongly at the household level in the present cohort, and should be directly compared to other cohorts.

INTRODUCTION

Globally, the number of people with diabetes is increasing rapidly, and in Sub-Saharan African (SSA) countries like Uganda the numbers will more than double within the next two decades.[1] The majority (90-95%) of all diabetes is type 2 diabetes (T2D)[1]. Prevention or postponement of the onset of T2D in high risk individuals through a healthy diet, increased physical activity, and weight loss has been successfully established in randomized clinical trials from both high-income[2,3] and middle-income countries[4,5]. However, it remains unclear as to the best methods for the translation of such clinical proof-of-concept evidence into low-cost effective and feasible population-wide interventions, especially in low-income countries, where access to diabetes diagnostics and treatment is often limited.[6,7]

In settings where daily life is focused around the family, households may present an opportunity to target several individuals simultaneously. Most of the variation in the risk of T2D in high-income countries is explained by lifestyle and behavioural factors, or by the interaction of lifestyle behaviours with genetic factors,[8,9] and household members are likely to share lifestyle behaviours and to some extent genes. Shared daily environment may partly explain the observed resemblance between household members such as spouses in risk factors related to the development of T2D like obesity,[10,11] exercise levels,[12,13] raised blood pressure[11,13,14] and smoking.[13,14] Further, spouses of a person with T2D have been shown to have higher fasting plasma glucose[15,16] and higher risk of developing T2D as compared to individuals with no spousal history of T2D.[16,17] For familial relations that include a genetic relationship the degree of diabetes risk concordance[17] and resemblance in obesity,[18] glycaemic levels,[19] blood pressure levels[20] and aerobic fitness status[21] are consistently higher than for spouses or adoptees, likely due to a combination of genetic and shared environmental effects.

In SSA, a family or a household often consists of multiple members and types of relationships (dyads), especially in rural areas. Yet little is known about T2D risk factor resemblance among individuals sharing daily life in a low-income country in epidemiological transition. Therefore, the objective of this study was to investigate resemblance of T2D risk factors at household level and by type of familial dyadic relationship in a rural Ugandan community.

METHODS

Study design and setting

This cross-sectional study was part of a larger study examining households with and without a member with previously diagnosed T2D.[22] Data were collected between December 2012 and March 2013 in Kasese District, Uganda. The district is mountainous and agrarian, though substantial parts may not be cultivated because they are National Forest, National Park or water bodies[23]. The majority of the approximately 770,000 inhabitants (75.3%) live in rural areas[23] and around 80% is involved in crop production, with small scale farming being the main occupation for the villagers. The main crops include cassava, sweet potatoes, maize, and matoke (plantain), which are also the primary staple foods, and cash crops like coffee[24]. The majority of people live in houses made of mud or sun-dried bricks with an iron sheet roof, no electricity, and no piped water. Average household size is 5.3 individuals.[24] Kasese District has three hospitals - one public general hospital (Bwera District Hospital) and two private-not-for-profit hospitals. Diabetes and hypertension diagnostics and treatment are mainly available at hospital level and only free of charge in public facilities.[6] In 2012, the health services were severely understaffed, with only 405 out of 933 positions filled.[23] The doctor-to-patient ratio was 1:43,037 and the nurse-to-patient ratio was 1:12,662[23] as compared to the overall national ratios of 1:24,725 for doctor-to-patients and 1:11,000 for nurse-to-patients[25].

One hundred households were approached and ninety agreed to participate. Reasons for non-participation were lack of time. Of the 90 households, half included a person diagnosed with T2D, selected from diabetes patient records at the nearby hospital diabetes clinic. Households without diagnosed T2D were selected using a random sampling plan.[22] To be included in the study, the household should consist of at least two generations, have at least three individuals aged ≥13 years, and no member with diagnosed HIV/AIDS, type 1 diabetes, or active tuberculosis. Households were defined as people living together and sharing food on a daily basis. All members aged 13 years or above, who had lived in the household for more than three months prior to the visit by the survey team were invited to participate (response rate 97.5%). Details of sampling, inclusion and exclusion criteria are described elsewhere.[22]

Ethics

Prior to data collection, the households were visited, the overall aim of the project was verbally explained and an information leaflet was handed out. On the day of data collection, verbal information about the project was given again and the participants were given time to ask questions. Verbal and written consent was obtained from all participants who still agreed to participate. For participants below 18 years of age, written consent was obtained from the caretaker. The study was approved by the Uganda National Council of Science and Technology (ADM 154/212/01), Makerere University School of Medicine Research & Ethics Committee (REC-REF 2012-183), St.Francis Hospital Nsambya, and Kagando Hospital.

Procedures

After the initial presentation of the study, a household profile was developed, detailing family structure, members, dyads (relationship between every pair of members) and age. Dwelling elevation (meters above sea-level) was measured using a Garmin Trex10 (Garmin, UK). HbA1c (%) was measured using an Afinion AS100 Analyzer (Axis Shield PoC, Norway); values were presented as % and as converted to mmol/mol.[26] Dysglycaemia was defined as HbA1c≥42 mmol/mol (≥6%).[27] Blood pressure was measured three times in sitting position after at least 10 minutes of rest (Omron M6 HEM7211E, Kyoto, Japan). Hypertension was defined as a systolic blood pressure≥140 mm Hg, or a diastolic blood pressure≥90 mm Hg,[28] averaged over the last two blood pressure readings. Body weight measured using a flat scale (model 876, SECA, UK) and height measured using a portable stadiometer (Model 213, SECA UK) were used to calculate body mass index (BMI) as weight (kg)/height $(m)^2$. Underweight, normal weight, overweight and obesity were defined according to the World Health Organization (WHO) classifications for adults[29] and for adolescents aged from 13 to 19 years according to WHO Child Growth Standards.[30] For dyads where one member could be below 19 years of age (parent-offspring, siblings and grandparent-grandchild) a Z-score of height-for-age was calculated and used instead of height (cm) for both dyad members. The Z-score was calculated according to de Onis et al. (2007) and individuals ≥19 years of age were handled as the oldest category in the WHO Child Growth Reference.[30]

As a measure of aerobic fitness status, an eight-minute step test was conducted to estimate aerobic capacity (maximal oxygen uptake, VO_2-max [mlO_2/min/kg body weight]) and managed according to the Cambridge Protocol.[31] Fifty individuals did not perform/complete at least four minutes of the step test. In data analyses using fitness status as a continuous variable, these individuals were excluded, whereas in data analyses where fitness status was used as a dichotomous variable, the 50 individuals were coded as unfit with the exception of those who had recently given birth or had an acute illness (n=5).

Household socio-economic status (SES), and individual educational level, age, sex, disease status and smoking were assessed using questionnaires. Daily sitting time was assessed using a locally adapted version of the International Physical Activity Questionnaire (IPAQ).[32]

Statistical analysis

The amount of resemblance in T2D risk factors in individuals living within the same household was assessed calculating intraclass-correlation coefficients (ICC) with general mixed models with household as a random effect, adjusting for sex, age, SES and household size.

Dyadic relationships were restricted to spouses, parent-offspring, grandparent-grandchild and sibling dyads and analysed as distinguishable members based on sex for spousal dyads (husband dyad number one and wife dyad number two), birth order for sibling dyads (oldest sibling dyad number 1) and age for parent-offspring and grandparent-grandchild dyads (parent and grandparents as dyad number 1 respectively).[33] As non-independence was assumed, a mixed model was used to analyse the dyadic resemblance between the same risk factor in the two dyad members. Our primary analyses modelled the risk factors HbA1c, blood pressure, height, BMI, fitness status and sitting time, separately, in dyad member 2 as a function of the same risk factor in dyad member 1. Random effects were dyad member 1 (to account e.g. for a parent having more than one child) or household (to account for more than one of the same type of dyad occurring per household). For dyadic relationships, regression coefficient estimates were reported with 95% confidence intervals. Logistic regression with household as a random effect was used to calculate the odds ratio (OR) of an individual having a condition if someone else in the household had the same condition. ORs are reported with 95% confidence intervals. Explanatory variables were introduced sequentially: individual level (sex,

age); dyad level (age-difference between the dyad members); and household level (socio-economic status, elevation of the dwelling, household size). Statistical significance was set as $p<0.05$.

For analyses including HbA1c, individuals with diagnosed T2D (n=45) were excluded and for analyses including blood pressure measures, individuals with diagnosed hypertension (n=32) were excluded as medication may have influenced these values. All statistical analyses were performed using Stata 14.1 SE (StataCorp LP USA).

RESULTS

From the 90 households we identified a total of 947 dyads of which 91 (9.6%) were spouses, 283 (29.8%) were parent-offspring dyads, 97 (10.2%) were grandparent-grandchild dyads and 148 (15.6%) were sibling dyads. The remaining 330 dyads were primarily in-laws and uncle/aunt-nephew/niece dyads (not included in this analysis). General characteristics and cardio-metabolic risk factors at household level and by dyadic relationship are summarized in Table 1. In 84 (93.3%) households, all meals were eaten within the household. Median dwelling elevation was 1,177 meters above sea-level (range 951-1,742 MSL).

Household resemblance in T2D risk factors

At household level ICCs showed statistically significant household member resemblance for four risk factors. After adjustment for age and sex, ICCs were statistically significant for fitness status (ICC=0.24, $p<0.001$), HbA1c (ICC=0.18, $p<0.001$), BMI (ICC=0.08, $p=0.010$) and systolic blood pressure (ICC=0.11, $p=0.003$), while only a tendency was observed for diastolic blood pressure (ICC=0.06, $p=0.06$). Additional adjustment for SES, household size or dwelling elevation did not change the ICCs.

Dyad resemblance

Dyad resemblance in T2D risk factors is shown as regression coefficients adjusted for age-difference and sex in Table 2. Sibling and parent-offspring dyads both had five statistically associated risk factors. Siblings were associated in measures of HbA1c, systolic blood pressure, diastolic blood pressure, height and fitness status, while parent-offspring dyads were associated with in HbA1c, systolic blood pressure, height, fitness status and sitting time.

Table 1. General characteristics and cardio-metabolic risk factors at household level and by dyadic relationships

(n)	Households (90)	Dyads by type (n)											
		Spouses (91)		Parents-offspring (283)				Grandparents-grandchildren (97)				Siblings (148)	
Members (n unique)		Wives (91)	Husbands (89)	Parents (150)		Offspring (164)		Grandparents (64)		Grandchildren (64)		Sisters (79)	Brothers (71)
				Mothers (88)	*Fathers (62)*	*Daughters 81*	*Sons (83)*	*Grandmothers (41)*	*Grandfathers (23)*	*Granddaughters (25)*	*Grandsons (39)*		
Individuals in household	5 (range 3-10)												
Age (Years)*	38.7 [33.0;43.1]	51.0 [42.7;57.4]	56.1 [49.6;67.4]	53.7 [47.6;63.1]	60.4 [52.6;68.4]	21.3 [15.8;30.7]	19.7 [16.0;26.7]	67.5 [56.6;72.7]	68.4 [60.5;74.7]	16.8 [13.8;18.8]	16.8 [14.6;19.5]	21.5 [15.4;39.6]	19.0 [16.5;24.0]
Age-difference (years)*[1]	46.0 [38.7;54.0]	6.1 [3.0;11.0]			32.6 [27.0;38.2]				50.2 [41.7;56.0]			4.8 [3.0;8.0]	
Diagnosed T2D n (%)	45 (50)	9 (9.9)	29 (32.6)	12 (13.6)	23 (37.1)	2 (2.5)	1 (1.2)	8 (19.5)	6 (26.1)	0 (0)	0 (0)	3 (3.8)	1 (1.4)
Dysglycaemia, n (%)	22 (24.4)	12(13.2)	5 (5.6)	11 (12.5)	4 (6.5)	5 (6.2)	1 (1.2)	6 (14.6)	2 (8.7)	1 (4.0)	0 (0)	8 (10.1)	1 (1.4)
Diagnosed Hypertension n (%)	28 (31.1)	10 (11.0)	14 (15.7)	12 (13.6)	10 (16.1)	0 (0)	0 (0)	12 (29.3)	6 (26.1)	0 (0)	0 (0)	2 (2.5)	1 (1.4)
Undiagnosed Hypertension n (%)	67 (74.4)	16 (17.6)	23 (26.1)	17 (19.5)	20 (32.8)	3 (3.7)	3 (3.6)	8 (19.5)	10 (45.5)	0 (0)	0 (0)	3 (3.9)	1 (1.4)
HbA1c (%)	5.4 (0.3)	5.5 (0.5)	5.4 (0.5)	5.6 (0.5)	5.5 (0.6)	5.4 (0.4)	5.3 (0.5)	5.7 (0.4)	5.6 (0.8)	5.4 (0.3)	5.3 (0.3)	5.4 (0.5)	5.3 (0.4)
(mmol/mol)[2]	35.4 (3.2)	36.9 (5.5)	35.8 (5.9)	37.3 (5.5)	36.4 (6.5)	35.0 (4.4)	34.6 (5.7)	38.3 (4.9)	38.0 (8.7)	35.9 (3.0)	34.4 (3.8)	36.0 (5.3)	34.4 (4.2)
Systolic blood pressure (mmHg)*[3]	128 [123;137]	134 [117;149]	139 [127;164]	137 [118;155]	151 [132;170]	118 [112;129]	124 [117;131]	152 [134;167]	164 [153;192]	117 [112;125]	125 [114;131]	120 [113;131]	122 [117;130]
Diastolic blood pressure (mmHg)*[3]	78 [74;82]	80 [74;89]	84 [76;92]	84 [79;91]	87 [79;95]	75 [71;81]	72 [69;80]	86 [73;91]	91 [79;94]	73 [66;78]	73 [66;78]	75 [70;81]	72 [66;78]
Height (cm)	155.2 (3.8)	152.4 (5.4)	161.3 (5.3)	151.5 (5.1)	160.6 (5.3)	153.5 (6.6)	158.4 (8.4)	150.4 (5.2)	159.0 (4.5)	153.3 (6.7)	156.3 (10.1)	152.7 (6.2)	160.3 (7.7)
Short stature n (%)[4,5]	78 (86.7)	30 (32.8)	49 (55.7)	33 (37.5)	38 (61.3)	19 (23.5)	45 (54.2)	22 (53.7)	15 (68.2)	3 (12.0)	20 (52.3)	19 (24.1)	35 (49.3)
Body mass index*[5]	21.7 [20.7;23.2]	23.1 [21.0;25.3]	21.5 [19.6;25.0]	22.4 [19.7;24.6]	22.1 [19.6;25.4]	22.4 [20.2;24.4]	20.4 [19.0;21.5]	21.2 [18.3;24.7]	21.0 [19.3;25.0]	20.8 [18.6;23.7]	19.9 [18.3;21.2]	22.4 [19.8;24.8]	19.2 [19.2;21.6]
Underweight n (%)	27 (30.0)	9 (9.9)	8 (9.1)	13 (14.8)	6 (9.7)	5 (6.2)	2 (2.4)	11 (26.8)	3 (13.6)	1 (4.0)	1 (2.6)	4 (5.1)	1 (1.4)
Overweight n (%)	52 (57.8)	25 (27.5)	24 (27.3)	19 (21.6)	20 (32.3)	19 (23.5)	5 (6.0)	10 (24.4)	6 (27.3)	4 (16.0)	0	21 (26.6)	2 (2.8)
Fitness status (VO2-max: ml O_2/min/kg)[6]	38.5 (4.7)	34.3 (6.8)	33.5 (8.8)	32.0 (6.7)	32.7 (7.2)	37.3 (6.6)	44.6 (6.8)	29.1 (6.8)	29.2 (6.0)	38.9 (5.9)	46.0 (4.6)	37.0 (7.0)	44.8 (5.9)
Unfit n (%)[7]	72 (80.0)	35 (40.2)	39 (44.3)	43 (49.4)	25 (41.0)	24 (29.6)	30 (36.1)	30 (75.0)	14 (63.6)	5 (20.0)	15 (39.5)	26 (32.9)	25 (35.2)
Sitting per day (min)*	275.4 [225;310]	208 [169;279]	274 [189;351]	231 [189;334]	283 [197;373]	261 [204;326]	240 [189;369]	274 [197;380]	257 [189;343]	274 [180;334]	240 [159;360]	257 [204;326]	238 [180;354]
Smoking status n (%)													
Never smoked	52 (57.8)	71 (78.0)	59 (66.3)	57 (64.8)	39 (62.9)	77 (95.1)	68 (81.9)	22 (53.7)	13 (56.5)	24 (96.0)	38 (97.4)	70 (88.6)	59 (83.1)
Former smoker	38 (42.2)	11 (12.1)	21 (23.6)	19 (21.6)	17 (27.4)	2 (2.5)	9 (10.8)	13 (31.7)	6 (26.1)	0 (0)	0 (0)	5 (6.3)	6 (8.5)
Current smoker	21 (23.3)	9 (9.9)	9 (10.1)	12 (13.6)	6 (9.7)	2 (2.5)	6 (7.2)	6 (14.6)	4 (17.4)	1 (4.0)	1 (2. 6)	4 (5.1)	6 (8.5)
Years of education*	5.3 (2.2)	2 [0;6]	6 [3;7]	2 [0;4)	5 [1;7]	6 [5;10]	7 [5;10]	0 [0;2]	5 [1;6]	6 [5;7]	6 [4;8]	6 [3:9]	7 [5;10]

Data are presented as mean (SD). *Median [p25;p75]]. [1]At household level age-difference is between the oldest and youngest individual in the household. [2]Individuals with diagnosed diabetes are excluded. [3]Individuals with diagnosed hypertension are excluded. [4]Short stature is defined as age (months) z-score below -2SD or final height for males below 161.9cm and for females below 150.1cm [30]. [5]Missing value on 1 man. [6]50 individuals did not complete the steptest. [7]Data missing on six individuals because of pregnancy, recent delivery, sickness, or technical error.

Table 2. Dyad regression coefficients for type 2 diabetes risk factors (adjusted for age-difference and sex)

(n)	Spouses (91)	Parents-offspring (283)	Grandparents-grandchildren (97)	Siblings (148)
HbA1c (%)[1]	0.18 [-0.09;0.45]	0.16* [0.02;0.29]	0.07 [-0.8;0.22]	0.28* [0.13;0.44]
Systolic Blood Pressure (mmHg)[2]	0.27* [0.01;0.53]	0.10* [0.04;0.16]	0.08 [-0.02;0.19]	0.18* [0.01;0.36]
Diastolic Blood pressure (mmHg)[2]	0.10 [-0.13;0.34]	0.02 [-0.07;0.10]	0.14* [0.02;0.27]	0.16* [0.01;0.32]
Height (cm or SD)[4]	0.07 [-0.13;0.26]	0.35* [0.19;0.52]	0.10 [-0.17;0.38]	0.26* [0.09;0.42]
Body mass index (kg/m^2)	0.19 [-0.04;0.42]	0.02 [-0.07;0.12]	-0.01 [-0.14;0.13]	0.11 [-0.06;0.29]
Fitness status ($mlO_2/min/kg$)[3]	0.42* [0.25;0.59]	0.46* [0.31;0.60]	-0.08 [-0.37;0.20]	0.38* [0.22;0.53]
Daily sitting time (minutes)	0.09 [-0.05;0.24]	0.15* [0.04;0.27]	0.10 [-0.07;0.27]	0.09 [-0.08;0.27]

Values are presented as regression coefficients [95% conf. interval]. Coefficients express the difference in each risk factor in dyad member 2 per unit difference in that same risk factor in dyad member one. *p<0.05. [1]Individuals with diagnosed diabetes were excluded. [2]Individuals with diagnosed hypertension were excluded. [3]In 15% of the dyads, one member did not complete the step test. [4]For spouses, height (cm) is used while for parents-offspring, grandparents-grandchildren and siblings, height-for-age is used and not adjusted for age-difference or sex.

Spouses were statistically significantly associated in systolic blood pressure and fitness status, while grandparent-grandchild dyads were only associated with regard to diastolic blood pressure. None of the four dyad types had a statically significant association for BMI.

Standardized regression coefficients are shown in Table 3. For spouses, parent-offspring and sibling dyads the standardized regression coefficients were highest for fitness status.

Table 3. Standardized regression coefficients for type 2 diabetes risk factors (adjusted for age-difference and sex)

	Spouses (91)	Parents-offspring (283)	Grandparents-grandchildren (97)	Siblings (148)
HbA1c[1]	0.19 [-0.11;0.50]	0.21* [0.02;0.40]	0.12 [-0.13;0.37]	0.26* [0.11;0.42]
Systolic Blood Pressure[2]	0.28* [0.01;0.54]	0.20* [0.08;0.33]	0.22 [-0.06;0.50]	0.20* [0.01;0.39]
Diastolic Blood pressure[2]	0.10 [-0.14;0.35]	0.02 [-0.11;0.15]	0.27* [0.03;0.05]	0.20* [0.01;0.39]
Height for age[4]	0.07 [-0.13;0.28]	0.26* [0.14;0.37]	0.08 [-0.13;0.31]	0.26* [0.09;0.42]
Body mass index	0.16 [-0.04;0.37]	0.02 [-0.11;0.16]	0.02 [-0.20;0.24]	0.14 [-0.03;0.31]
VO_2-max[3]	0.54* [0.32;0.76]	0.41* [0.28;0.54]	-0.09 [-0.38; 0.21]	0.41* [0.25;0.57]
Daily sitting time	0.11 [-0.09;0.31]	0.17* [0.04;0.32]	0.11 [-0.09;0.32]	0.09 [-0.10;0.27]

Values are presented as standardized regression coefficients [95% conf. interval]. *p<0.05

Concordance in risk factors

The results of the logistic regression models are shown in Table 4. At household level, effect estimates showed that if one member in the household had dysglycaemia, the OR of another household member having the same status was increased almost 20 times. Having diagnosed hypertension in the household increased the odds of another member having diagnosed or undiagnosed hypertension 2.6 times, whereas undiagnosed hypertension increased the odds of diagnosed or undiagnosed hypertension in another member 4.8 times. The ORs of being overweight or obese, underweight, unfit, smoker or former smoker were all statistically significantly higher if another member of the household had the same status as compared to if no one in the household had the same status (Table 4).

Table 4. Odds ratios of having a condition as a function of the disease or risk factor status in other members of the same household (adjusted for age, sex and household size)

Exposure (status	Outcome	Household level
Diagnosed diabetes	*Dysglycaemia*	0.8 [0.4; 2.0]
Dysglycaemia	*Dysglycaemia*	19.8 [11.0; 35.5]*
Diagnosed hypertension	*Diagnosed or undiagnosed hypertension*	2.6 [1.5; 4.5]*
Undiagnosed hypertension	*Diagnosed or undiagnosed hypertension*	4.8 [2.9; 8.0]*
Short stature	*Short stature*	10.9 [6.9; 17.0]*
Overweight or obesity	*Overweight or obesity*	9.0 [6.1; 13.2]*
Underweight	*Underweight*	13.7 [7.1; 26.3]*
Unfit	*Unfit*[5]	11.2 [7.4; 17.1]*
Smoker	*Smoker*	33.7 [15.8; 71.8]*
Former smoker	*Former smoker*	18.9 [9.4; 38.0]*

Values are presented as odds ratios [95% conf. interval]. *p<0.05. [1]Individuals with diagnosed diabetes were excluded. [2]Individuals with diagnosed hypertension were excluded. [3]In 15% of the dyads, one member did not complete the step test. [4]Not adjusted for age-difference. [5]Unfit is defined as a fitness level below middle derived from VO_2-max and grouped according to Astrand (1960).[34]

DISCUSSION

The results of the present study indicate that individuals living in the same household in rural Uganda share risk factors for T2D and cardio-metabolic diseases. We showed that, in particular for systolic blood pressure and fitness status, the spousal association was at least as strong as the association between siblings or parent-offspring pairs, indicating an effect of shared lifestyle behaviours. For other cardio-metabolic risk

factors the resemblance was more prominent between siblings and parent-offspring dyads, whereas grandparent-grandchild dyads were less alike.

To our knowledge this is the first study to investigate the resemblance of multiple cardio-metabolic risk factors in household clusters including several generations living and eating together on a daily basis. A German study of aerobic fitness found an ICC of 0.22 in fitness status in nuclear families, but no association when restricting the analyses to spouses.[35] Our findings of dyad resemblance in HbA1c, blood pressure, height and fitness status are in agreement with other epidemiological studies focusing on a single type of dyad[19, 20] or a single type of risk factor.[35,36] We are not aware of studies from low-income countries investigating household or dyad resemblance in risk factors for T2D.

Among the measured risk factors, fitness status had the highest ICC at household level and standardised regression coefficient among spouse, parent-offspring and sibling dyads. The high resemblance in fitness status is partly explained by the high heritability of VO_2-max.[21] However, in contrast to the German study[35] we also found a high association in spousal fitness status suggesting that also shared physical activity patterns may contribute to the high fitness status resemblance in our study population. In the Ugandan situation, a peasant's wife is most often also a peasant, and offspring help cultivating the family land. Shared daily activities as the explanation for spousal resemblance in fitness status is supported by a French study finding that spouses' physical activity patterns were only similar during weekend days.[37] In addition, walking was the primary means of transportation for most of the study participants, giving all individuals in the same household the same walking distance and elevation differential when e.g. going to the nearest trading centre. However, adjusting for elevation gave only a modest attenuation of the household ICC or the dyad resemblance in fitness status.

In line with the results of a meta-analysis,[38] spouses resembled each other with regard to systolic blood pressure. Contradicting other studies[10,38] we did not find a statistically significant spousal association for BMI, diastolic blood pressure or HbA1c. Discordance in ethnicity of spouses, low numbers of people living in the household and higher SES have previously been shown to attenuate the spousal association in BMI.[10] However, none of these factors were present or affected the absence of a spousal

BMI association on our study. Assortative mating and/or convergence over time are often used to explain spousal resemblance in risk factors for T2D.[12,39] However, studies of assortative mating and risk factors for T2D are almost exclusively from high-income settings, and preferences for choice of spouse may differ across geographical, social and ethnic settings. For instance, overweight has traditionally been viewed as a desirable feature in SSA settings[40] whereas it is more stigmatizing in high-income settings.[41] Further, until recently the prevalence of obesity in SSA was low, and results from a Danish study showed a tendency to an increase in assorted marriages between obese spouses along with the obesity epidemic.[39]

In contrast to other studies of genetically related individuals, we did not find a relationship in BMI for parent-offspring[18,42] or sibling dyads.[19,36,43] Concerning parent-offspring, a study from the U.S including children from 2-16 years of age suggested that pubertal children are less likely to resemble their parents in BMI than pre-puberty children, as they grow more independent of parents' eating and exercise behaviours.[42] This could explain the lack of parent-offspring relationship in our study where some of the parent-offspring dyads included adult offspring. However, stratifying parent-offspring dyads into adolescents and adult offspring or above/below median age-difference did not change the lack of statistical associations. In terms of siblings, other studies found that sibling dyads resembled in BMI,[19] but that the sibling BMI correlations were less pronounced during adolescence,[36] decreased with increasing age difference[19] and were higher among home living adolescents than adult siblings living apart.[43] The mean sibling age difference (7 years) in our study was not markedly different from the mentioned studies, and the siblings lived together. Thus, these factors cannot entirely explain the lack of relationship.

The last relationship with a genetic component examined in the present study was grandparent-grandchild dyads. Again no relationship was seen in BMI, which is supported by data from a Korean population,[44] but in contrast to a study from Belgium finding a direct association in obesity measures through three generations.[45] Neither the Korean nor the Belgian study reported that grandparents and grandchildren lived together, which they did in our study and could have increased the chance of resemblance in BMI. However, Uganda is a country in transition in terms of both disease burden and nutrition. In addition, the Ruwenzori Mountain region in Kasese district was the centre of civil strife with a

civil war in 1962-1982 and again from 1996-2002, making it likely that grandparents and grandchildren were exposed to very different intrauterine environments and growth conditions. This hypothesis is supported by the findings of a statistically significant height increment between each of the three generations in our cohort (data not shown), which was not reported in the study from Korea including three generations.[44] Potential unmeasured confounders for BMI may have been unreported/undiagnosed infectious disease such as tuberculosis or HIV/AIDS; both have a fairly high prevalence in the study setting[46] and both affect body weight.

The high ORs in smoking status may partly be explained by a low overall smoking prevalence (7.6%). Further, 63% of the smokers lived together with at least one other smoker. The high resemblance in smoking status is supported by results of studies finding a high spousal resemblance in smoking status[12] and that both smoking and quitting smoking spread in social ties in social networks.[47]

Strengths and limitations

One of the main strengths of this study is the household-based approach. Visiting the families in the home setting resulted in a high individual response rate (97.5%) and thus only minimal risk of selection bias in dyad representativeness. The cross-sectional design prevents us from concluding on whether the spousal resemblance was due to shared risk behaviours or assortative mating, and for the genetic relationships, we cannot distinguish between shared genes and shared environment/behaviours. The ICCs reflect the proportion of variances, whereby the sizes of the ICCs cannot be compared to other cohorts or settings. Thus, the size of ICCs should only be interpreted as a tool to investigate which risk factors resemble most strongly at the household level in the present cohort. The application of HbA1c as a diagnostic tool in African populations is debated [48]. However, in the present study, HbA1c was used to investigate resemblance in dyad members and not to diagnose diabetes. Due to the initial sampling of this study population, 50% of the households had a member with diagnosed T2D. We have previously shown that having diagnosed T2D in the household may have positive spill-over effects on the other members[22] potentially due to changes in diet and physical activity due to the diabetes status.[49] This could explain the difference between diagnosed T2D and dysglycaemia in the household as a risk factor for dysglycaemia in other members of the household.

CONCLUSION

The moderate to strong correlations in T2D risk factors at household level and between spouses, parent-offspring, and sibling dyads suggest that shared behavioural and environmental factors such as physical activity may influence the risk factor level among cohabiting individuals. The marked degree of household resemblance for certain T2D risk factors highlights the potential of the household setting for screening and prevention of T2D. Thus when one household member presents with elevated glucose, blood pressure, or physical inactivity, the entire household could benefit from lifestyle interventions.

Acknowledgement

We thank the people who opened their homes and took time to participate in this study, the field assistants for collecting data and carrying equipment up the mountain slopes, and the Kagando Hospital staff members for their hospitality and support. We also thank Dr. Adam Hulman, Department of Public Health, University of Aarhus, for help with data management and Soren Brage, University of Cambridge, for assistance with step-test data.

Author contribution statement

Dr. Jannie Nielsen developed the study protocol, collected the data, performed the statistical analyses and the interpretation of data, and drafted, revised and finalized the article.

Dr. Silver K. Bahendeka contributed to the protocol with substantial knowledge concerning diabetes in Uganda and specifically in Kasese district, took part in the later stage and final interpretation of data, and participated in developing, revising and finalizing the manuscript.

Professor Susan R. Whyte contributed to the development of the study protocol, took part in the later stage and final interpretation of data, and participated in developing, revising and finalizing the manuscript.

Associate Professor Dan W. Meyrowitsch contributed to the development of the study protocol, took part in the later stage and final interpretation of data, and participated in developing, revising and finalizing the manuscript.

Professor Ib C. Bygbjerg contributed to the development of the study protocol, took part in the later stage and final interpretation of data, and participated in developing, revising and finalizing the manuscript.

Professor Daniel R. Witte performed the statistical analysis and the interpretation of data, and participated in developing, revising and finalizing the manuscript.

Competing interests

Dr. Nielsen's PhD fellowship was partly funded by Novo Nordisk Fonden (grant no. 29847).

Funding

The study was sponsored by University of Copenhagen, Thorvald Madsens Fond, Aase and Ejnar Danielsens Fond, and Christian and Otilia Brorsons Rejselegat. No sponsor had any influence on the study design, data collection, analysis, or interpretation or the writing of this article. The remaining authors have declared no conflict of interest.

Data sharing statement

No additional data available.

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STROBE CHECKLIST

Study: Household and familial resemblance in risk factors for type 2 diabetes and related cardio-metabolic diseases in rural Uganda

Type of study: Cross-sectional

	Item No	Recommendation	Page
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/ rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	5
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*6*
Bias	9	Describe any efforts to address potential sources of bias	5
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7
		(*b*) Describe any methods used to examine subgroups and interactions	7
		(*c*) Explain how missing data were addressed	6
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	9
		(b) Give reasons for non-participation at each stage	9
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8+9
		(b) Indicate number of participants with missing data for each variable of interest	9
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	10+11
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10+11
		(*b*) Report category boundaries when continuous variables were categorized	9
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	11
Discussion			
Key results	18	Summarise key results with reference to study objectives	12
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	13
Generalisability	21	Discuss the generalisability (external validity) of the study results	14+15
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	16

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Household and familial resemblance in risk factors for type 2 diabetes and related cardio-metabolic diseases in rural Uganda: A cross-sectional community sample

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2016-015214.R2
Article Type:	Research
Date Submitted by the Author:	21-Jul-2017
Complete List of Authors:	Nielsen, Jannie ; University of Copenhagen, Global Health Section, Department of Public Health Bahendeka, Silver; St. Francis Hospital Nsambya, Whyte, Susan; University of Copenhagen, Department of Anthropology Meyrowitsch, Dan; University of Copenhagen, Global Health Section, Department of Public Health Bygbjerg, Ib; University of Copenhagen, Global Health Section, Department of Public Health Witte, Daniel; University of Aarhus, Department of Public Health; Danish Diabetes Academy
Primary Subject Heading:	Public health
Secondary Subject Heading:	Global health, Diabetes and endocrinology, Epidemiology
Keywords:	PUBLIC HEALTH, General diabetes < DIABETES & ENDOCRINOLOGY, EPIDEMIOLOGY

Household and familial resemblance in risk factors for type 2 diabetes and related cardio-metabolic diseases in rural Uganda: A cross-sectional community sample

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Word count: 3304

ABSTRACT

OBJECTIVES

Prevention of type 2 diabetes (T2D) has been successfully established in randomized clinical trials. However, the best methods for the translation of this evidence into effective population-wide interventions remain unclear. To assess whether households could be a target for T2D prevention and screening, we investigated the resemblance of T2D risk factors at household level and by type of familial dyadic relationship in a rural Ugandan community.

METHODS

This cross-sectional household based study included 437 individuals ≥13 years of age from 90 rural households in south-western Uganda. Resemblance in HbA1c, anthropometry, blood pressure, fitness status and sitting time were analysed using a general mixed model with random effects (by household or dyad) to calculate household intraclass-correlation coefficients (ICC) and dyadic regression coefficients. Logistic regression with household as a random effect was used to calculate the odds ratios (ORs) for individuals having a condition or risk factor if another household member had the same condition.

RESULTS

The strongest degree of household member resemblances in T2D risk factors was seen in relation to fitness status (ICC=0.24), HbA1c (ICC=0.18), and systolic blood pressure (ICC=0.11). Regarding dyadic resemblance, the highest standardised regression coefficient was seen in fitness status for spouses (0.54 95%CI:0.32;0.76), parent-offspring (0.41 95%CI:0.28;0.54) and siblings (0.41 95%CI:0.25;0.57). Overall, parent-offspring and sibling pairs were the dyads with strongest resemblance, followed by spouses.

CONCLUSIONS

The marked degree of resemblance in T2D risk factors at household level and between spouses, parent-offspring, and sibling dyads suggest that shared behavioural and environmental factors may influence risk factor levels among cohabiting individuals, which point to the potential of the household setting for screening and prevention of T2D.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- The household-based approach, which involved visiting the families in the home setting, resulted in a high individual response rate (97.5%) and thus only minimal risk of selection bias in dyad representativeness.
- The study included a comprehensive set of risk factor measurements and four types of dyadic relationships, which enabled us to investigate resemblance in multiple risk factors for type 2 diabetes in genetic and non-genetic relationships and across generations.
- The cross-sectional design prevents us from concluding on whether the spousal resemblance was due to shared risk behaviours or assortative mating, and for the genetic relationships we cannot distinguish between shared genes and shared environment/behaviours.
- The size of the intraclass-correlation coefficients should only be interpreted as a tool to investigate which risk factors resemble most strongly at the household level in the present cohort, and should be directly compared to other cohorts.

INTRODUCTION

Globally, the number of people with diabetes is increasing rapidly, and in Sub-Saharan African (SSA) countries like Uganda the numbers will more than double within the next two decades.[1] The majority (90-95%) of all diabetes is type 2 diabetes (T2D)[1]. Prevention or postponement of the onset of T2D in high risk individuals through a healthy diet, increased physical activity, and weight loss has been successfully established in randomized clinical trials from both high-income[2,3] and middle-income countries[4,5]. However, it remains unclear as to the best methods for the translation of such clinical proof-of-concept evidence into low-cost effective and feasible population-wide interventions, especially in low-income countries, where access to diabetes diagnostics and treatment is often limited.[6,7]

In settings where daily life is focused around the family, households may present an opportunity to target several individuals simultaneously. Most of the variation in the risk of T2D in high-income countries is explained by lifestyle and behavioural factors, or by the interaction of lifestyle behaviours with genetic factors,[8,9] and household members are likely to share lifestyle behaviours and to some extent genes. Shared daily environment may partly explain the observed resemblance between household members such as spouses in risk factors related to the development of T2D like obesity,[10,11] exercise levels,[12,13] raised blood pressure[11,13,14] and smoking.[13,14] Further, spouses of a person with T2D have been shown to have higher fasting plasma glucose[15,16] and higher risk of developing T2D as compared to individuals with no spousal history of T2D.[16,17] For familial relations that include a genetic relationship the degree of diabetes risk concordance[17] and resemblance in obesity,[18] glycaemic levels,[19] blood pressure levels[20] and aerobic fitness status[21] are consistently higher than for spouses or adoptees, likely due to a combination of genetic and shared environmental effects.

In SSA, the number of people with diabetes is increasing in both urban and rural areas. However, especially in the rural areas is access to diabetes diagnostics and treatment very restricted[6,7]. Thus, novel approaches to low-cost diabetes prevention in such settings is highly needed. In SSA, a family or a household often consists of multiple members and types of relationships (dyads), especially in rural areas. Yet little is known about T2D risk factor resemblance among individuals sharing daily life in a low-income country in

epidemiological transition. Therefore, the objective of this study was to investigate resemblance of T2D risk factors at household level and by type of familial dyadic relationship in a rural Ugandan community.

METHODS

Study design and setting

This cross-sectional study was part of a larger study examining households with and without a member with previously diagnosed T2D.[22] Data were collected between December 2012 and March 2013 in Kasese District, Uganda. The district is mountainous and agrarian, though substantial parts may not be cultivated because they are National Forest, National Park or water bodies[23]. The majority of the approximately 770,000 inhabitants (75.3%) live in rural areas[23] and around 80% is involved in crop production, with small scale farming being the main occupation for the villagers. The main crops include cassava, sweet potatoes, maize, and matoke (plantain), which are also the primary staple foods, and cash crops like coffee[24]. The majority of people live in houses made of mud or sun-dried bricks with an iron sheet roof, no electricity, and no piped water. Average household size is 5.3 individuals.[24] Kasese District has three hospitals - one public general hospital (Bwera District Hospital) and two private-not-for-profit hospitals. Diabetes and hypertension diagnostics and treatment are mainly available at hospital level and only free of charge in public facilities.[6] In 2012, the health services were severely understaffed, with only 405 out of 933 positions filled.[23] The doctor-to-patient ratio was 1:43,037 and the nurse-to-patient ratio was 1:12,662[23] as compared to the overall national ratios of 1:24,725 for doctor-to-patients and 1:11,000 for nurse-to-patients[25].

One hundred households were approached and ninety agreed to participate. Reasons for non-participation were lack of time. Of the 90 households, half included a person diagnosed with T2D, selected from diabetes patient records at the nearby hospital diabetes clinic. Households without diagnosed T2D were selected using a random sampling plan.[22] To be included in the study, the household should consist of at least two generations, have at least three individuals aged ≥13 years, and no member with diagnosed HIV/AIDS, type 1 diabetes, or active tuberculosis. Households were defined as people living together and sharing food on a daily basis. All members aged 13 years or above, who had lived in the household for more

than three months prior to the visit by the survey team were invited to participate (response rate 97.5%). Details of sampling, inclusion and exclusion criteria are described elsewhere.[22]

Ethics

Prior to data collection, the households were visited, the overall aim of the project was verbally explained and an information leaflet was handed out. On the day of data collection, verbal information about the project was given again and the participants were given time to ask questions. Verbal and written consent was obtained from all participants who still agreed to participate. For participants below 18 years of age, written consent was obtained from the caretaker. The study was approved by the Uganda National Council of Science and Technology (ADM 154/212/01), Makerere University School of Medicine Research & Ethics Committee (REC-REF 2012-183), St.Francis Hospital Nsambya, and Kagando Hospital.

Procedures

After the initial presentation of the study, a household profile was developed, detailing family structure, members, dyads (relationship between every pair of members) and age. Dwelling elevation (meters above sea-level) was measured using a Garmin Trex10 (Garmin, UK). HbA1c (%) was measured using an Afinion AS100 Analyzer (Axis Shield PoC, Norway); values were presented as % and as converted to mmol/mol.[26] Dysglycaemia was defined as HbA1c≥42 mmol/mol (≥6%).[27] Blood pressure was measured three times in sitting position after at least 10 minutes of rest (Omron M6 HEM7211E, Kyoto, Japan). Hypertension was defined as a systolic blood pressure≥140 mm Hg, or a diastolic blood pressure≥90 mm Hg,[28] averaged over the last two blood pressure readings. Body weight measured using a flat scale (model 876, SECA, UK) and height measured using a portable stadiometer (Model 213, SECA UK) were used to calculate body mass index (BMI) as weight (kg)/height $(m)^2$. Underweight, normal weight, overweight and obesity were defined according to the World Health Organization (WHO) classifications for adults[29] and for adolescents aged from 13 to 19 years according to WHO Child Growth Standards.[30] For dyads where one member could be below 19 years of age (parent-offspring, siblings and grandparent-grandchild) a Z-score of height-for-age was calculated and used instead of height (cm) for both dyad members. The Z-score was

calculated according to de Onis et al. (2007) and individuals ≥19 years of age were handled as the oldest category in the WHO Child Growth Reference.[30]

As a measure of aerobic fitness status, an eight-minute step test was conducted to estimate aerobic capacity (maximal oxygen uptake, VO_2-max [mlO_2/min/kg body weight]) and managed according to the Cambridge Protocol.[31] Fifty individuals did not perform/complete at least four minutes of the step test. In data analyses using fitness status as a continuous variable, these individuals were excluded, whereas in data analyses where fitness status was used as a dichotomous variable, the 50 individuals were coded as unfit with the exception of those who had recently given birth or had an acute illness (n=5).

Household socio-economic status (SES), and individual educational level, age, sex, disease status and smoking were assessed using questionnaires. Daily sitting time was assessed using a locally adapted version of the International Physical Activity Questionnaire (IPAQ).[32]

Statistical analysis

The amount of resemblance in T2D risk factors in individuals living within the same household was assessed calculating intraclass-correlation coefficients (ICC) with general mixed models with household as a random effect, adjusting for sex, age, SES and household size.

Dyadic relationships were restricted to spouses, parent-offspring, grandparent-grandchild and sibling dyads and analysed as distinguishable members based on sex for spousal dyads (husband dyad number one and wife dyad number two), birth order for sibling dyads (oldest sibling dyad number 1) and age for parent-offspring and grandparent-grandchild dyads (parent and grandparents as dyad number 1 respectively).[33] As non-independence was assumed, a mixed model was used to analyse the dyadic resemblance between the same risk factor in the two dyad members. Our primary analyses modelled the risk factors HbA1c, blood pressure, height, BMI, fitness status and sitting time, separately, in dyad member 2 as a function of the same risk factor in dyad member 1. Random effects were dyad member 1 (to account e.g. for a parent having more than one child) or household (to account for more than one of the same type of dyad occurring per household). For dyadic relationships, regression coefficient estimates were reported with 95% confidence intervals. Logistic regression with household as a random effect was used to calculate the odds ratio (OR) of

an individual having a condition if someone else in the household had the same condition. ORs are reported with 95% confidence intervals. Explanatory variables were introduced sequentially: individual level (sex, age); dyad level (age-difference between the dyad members); and household level (socio-economic status, elevation of the dwelling, household size). Statistical significance was set as $p<0.05$.

For analyses including HbA1c, individuals with diagnosed T2D (n=45) were excluded and for analyses including blood pressure measures, individuals with diagnosed hypertension (n=32) were excluded as medication may have influenced these values. All statistical analyses were performed using Stata 14.1 SE (StataCorp LP USA).

RESULTS

From the 90 households we identified a total of 947 dyads of which 91 (9.6%) were spouses, 283 (29.8%) were parent-offspring dyads, 97 (10.2%) were grandparent-grandchild dyads and 148 (15.6%) were sibling dyads. The remaining 330 dyads were primarily in-laws and uncle/aunt-nephew/niece dyads (not included in this analysis). General characteristics and cardio-metabolic risk factors at household level and by dyadic relationship are summarized in Table 1. In 84 (93.3%) households, all meals were eaten within the household. Median dwelling elevation was 1,177 meters above sea-level (range 951-1,742 MSL).

Household resemblance in T2D risk factors

At household level ICCs showed statistically significant household member resemblance for four risk factors. After adjustment for age and sex, ICCs were statistically significant for fitness status (ICC=0.24, $p<0.001$), HbA1c (ICC=0.18, $p<0.001$), BMI (ICC=0.08, $p=0.010$) and systolic blood pressure (ICC=0.11, $p=0.003$), while only a tendency was observed for diastolic blood pressure (ICC=0.06, $p=0.06$). Additional adjustment for SES, household size or dwelling elevation did not change the ICCs.

Dyad resemblance

Dyad resemblance in T2D risk factors is shown as regression coefficients adjusted for age-difference and sex in Table 2. Sibling and parent-offspring dyads both had five statistically associated risk factors.

Siblings were associated in measures of HbA1c, systolic blood pressure, diastolic blood pressure, height

Table 1. General characteristics and cardio-metabolic risk factors at household level and by dyadic relationships

(n)	Households (90)	Dyads by type (n)[1]											
		Spouses (91)		Parents-offspring (283)				Grandparents-grandchildren (97)				Siblings (148)	
				Parents (150)		Offspring (164)		Grandparents (64)		Grandchildren (64)			
Members (n unique)		Wives (91)	Husbands (89)	*Mothers (88)*	*Fathers (62)*	*Daughters 81*	*Sons (83)*	*Grandmothers (41)*	*Grandfathers (23)*	*Granddaughters (25)*	*Grandsons (39)*	Sisters (79)	Brothers (71)
Individuals in household	5 (range 3-10)												
Age (Years)*	38.7 [33.0;43.1]	51.0 [42.7;57.4]	56.1 [49.6;67.4]	53.7 [47.6;63.1]	60.4 [52.6;68.4]	21.3 [15.8;30.7]	19.7 [16.0;26.7]	67.5 [56.6;72.7]	68.4 [60.5;74.7]	16.8 [13.8;18.8]	16.8 [14.6;19.5]	21.5 [15.4;39.6]	19.0 [16.5;24.0]
Age-difference (years)*[2]	46.0 [38.7;54.0]	6.1 [3.0;11.0]			32.6 [27.0;38.2]				50.2 [41.7;56.0]			4.8 [3.0;8.0]	
Diagnosed T2D n (%)	45 (50)	9 (9.9)	29 (32.6)	12 (13.6)	23 (37.1)	2 (2.5)	1 (1.2)	8 (19.5)	6 (26.1)	0 (0)	0 (0)	3 (3.8)	1 (1.4)
Dysglycaemia, n (%)	22 (24.4)	12(13.2)	5 (5.6)	11 (12.5)	4 (6.5)	5 (6.2)	1 (1.2)	6 (14.6)	2 (8.7)	1 (4.0)	0 (0)	8 (10.1)	1 (1.4)
Diagnosed Hypertension n (%)	28 (31.1)	10 (11.0)	14 (15.7)	12 (13.6)	10 (16.1)	0 (0)	0 (0)	12 (29.3)	6 (26.1)	0 (0)	0 (0)	2 (2.5)	1 (1.4)
Undiagnosed Hypertension n (%)	67 (74.4)	16 (17.6)	23 (26.1)	17 (19.5)	20 (32.8)	3 (3.7)	3 (3.6)	8 (19.5)	10 (45.5)	0 (0)	0 (0)	3 (3.9)	1 (1.4)
HbA1c (%)	5.4 (0.3)	5.5 (0.5)	5.4 (0.5)	5.6 (0.5)	5.5 (0.6)	5.4 (0.4)	5.3 (0.5)	5.7 (0.4)	5.6 (0.8)	5.4 (0.3)	5.3 (0.3)	5.4 (0.5)	5.3 (0.4)
(mmol/mol)[3]	35.4 (3.2)	36.9 (5.5)	35.8 (5.9)	37.3 (5.5)	36.4 (6.5)	35.0 (4.4)	34.6 (5.7)	38.3 (4.9)	38.0 (8.7)	35.9 (3.0)	34.4 (3.8)	36.0 (5.3)	34.4 (4.2)
Systolic blood pressure (mmHg)*[4]	128 [123;137]	134 [117;149]	139 [127;164]	137 [118;155]	151 [132;170]	118 [112;129]	124 [117;131]	152 [134;167]	164 [153;192]	117 [112;125]	125 [114;131]	120 [113;131]	122 [117;130]
Diastolic blood pressure (mmHg)*[5]	78 [74;82]	80 [74;89]	84 [76;92]	84 [79;91]	87 [79;95]	75 [71;81]	72 [69;80]	86 [73;91]	91 [79;94]	73 [66;78]	73 [66;78]	75 [70;81]	72 [66;78]
Height (cm)	155.2 (3.8)	152.4 (5.4)	161.3 (5.3)	151.5 (5.1)	160.6 (5.3)	153.5 (6.6)	158.4 (8.4)	150.4 (5.2)	159.0 (4.5)	153.3 (6.7)	156.3 (10.1)	152.7 (6.2)	160.3 (7.7)
Short stature n (%)[5,6]	78 (86.7)	30 (32.8)	49 (55.7)	33 (37.5)	38 (61.3)	19 (23.5)	45 (54.2)	22 (53.7)	15 (68.2)	3 (12.0)	20 (52.3)	19 (24.1)	35 (49.3)
Body mass index*[6]	21.7 [20.7;23.2]	23.1 [21.0;25.3]	21.5 [19.6;25.0]	22.4 [19.7;24.6]	22.1 [19.6;25.4]	22.4 [20.2;24.4]	20.4 [19.0;21.5]	21.2 [18.3;24.7]	21.0 [19.3;25.0]	20.8 [18.6;23.7]	19.9 [18.3;21.2]	22.4 [19.8;24.8]	19.2 [19.2;21.6]
Underweight n (%)	27 (30.0)	9 (9.9)	8 (9.1)	13 (14.8)	6 (9.7)	5 (6.2)	2 (2.4)	11 (26.8)	3 (13.6)	1 (4.0)	1 (2.6)	4 (5.1)	1 (1.4)
Overweight n (%)	52 (57.8)	25 (27.5)	24 (27.3)	19 (21.6)	20 (32.3)	19 (23.5)	5 (6.0)	10 (24.4)	6 (27.3)	4 (16.0)	0	21 (26.6)	2 (2.8)
Fitness status (VO2-max: ml O_2/min/kg)[7]	38.5 (4.7)	34.3 (6.8)	33.5 (8.8)	32.0 (6.7)	32.7 (7.2)	37.3 (6.6)	44.6 (6.8)	29.1 (6.8)	29.2 (6.0)	38.9 (5.9)	46.0 (4.6)	37.0 (7.0)	44.8 (5.9)
Unfit n (%)[8]	72 (80.0)	35 (40.2)	39 (44.3)	43 (49.4)	25 (41.0)	24 (29.6)	30 (36.1)	30 (75.0)	14 (63.6)	5 (20.0)	15 (39.5)	26 (32.9)	25 (35.2)
Sitting per day (min)*	275.4 [225;310]	208 [169;279]	274 [189;351]	231 [189;334]	283 [197;373]	261 [204;326]	240 [189;369]	274 [197;380]	257 [189;343]	274 [180;334]	240 [159;360]	257 [204;326]	238 [180;354]
Smoking status n (%)													
Never smoked	52 (57.8)	71 (78.0)	59 (66.3)	57 (64.8)	39 (62.9)	77 (95.1)	68 (81.9)	22 (53.7)	13 (56.5)	24 (96.0)	38 (97.4)	70 (88.6)	59 (83.1)
Former smoker	38 (42.2)	11 (12.1)	21 (23.6)	19 (21.6)	17 (27.4)	2 (2.5)	9 (10.8)	13 (31.7)	6 (26.1)	0 (0)	0 (0)	5 (6.3)	6 (8.5)
Current smoker	21 (23.3)	9 (9.9)	9 (10.1)	12 (13.6)	6 (9.7)	2 (2.5)	6 (7.2)	6 (14.6)	4 (17.4)	1 (4.0)	1 (2. 6)	4 (5.1)	6 (8.5)
Years of education*	5.3 (2.2)	2 [0;6]	6 [3;7]	2 [0;4)	5 [1;7]	6 [5;10]	7 [5;10]	0 [0;2]	5 [1;6]	6 [5;7]	6 [4;8]	6 [3:9]	7 [5;10]

Data are presented as mean (SD). *Median [p25;p75]]. [1]Please note that for the different types of dyads there can be a different number of dyad member 1 and dyad member 2 as e.g. one husband had two wives or a mother can have more than one child. [2]At household level age-difference is between the oldest and youngest individual in the household. [3]Individuals with diagnosed diabetes are excluded. [4]Individuals with diagnosed hypertension are excluded. [5]Short stature is defined as age (months) z-score below -2SD or final height for males below 161.9cm and for females below 150.1cm [30]. [6]Missing value on 1 man. [7]50 individuals did not complete the steptest. [8]Data missing on six individuals because of pregnancy, recent delivery, sickness, or technical error.

and fitness status, while parent-offspring dyads were associated with in HbA1c, systolic blood pressure, height, fitness status and sitting time.

Table 2. Dyad regression coefficients for type 2 diabetes risk factors (adjusted for age-difference and sex)

(n)	Spouses (91)	Parents-offspring (283)	Grandparents-grandchildren (97)	Siblings (148)
HbA1c (%)[1]	0.18 [-0.09;0.45]	0.16* [0.02;0.29]	0.07 [-0.8;0.22]	0.28* [0.13;0.44]
Systolic Blood Pressure (mmHg)[2]	0.27* [0.01;0.53]	0.10* [0.04;0.16]	0.08 [-0.02;0.19]	0.18* [0.01;0.36]
Diastolic Blood pressure (mmHg)[2]	0.10 [-0.13;0.34]	0.02 [-0.07;0.10]	0.14* [0.02;0.27]	0.16* [0.01;0.32]
Height (cm or SD)[4]	0.07 [-0.13;0.26]	0.35* [0.19;0.52]	0.10 [-0.17;0.38]	0.26* [0.09;0.42]
Body mass index (kg/m^2)	0.19 [-0.04;0.42]	0.02 [-0.07;0.12]	-0.01 [-0.14;0.13]	0.11 [-0.06;0.29]
Fitness status ($mlO_2/min/kg$)[3]	0.42* [0.25;0.59]	0.46* [0.31;0.60]	-0.08 [-0.37;0.20]	0.38* [0.22;0.53]
Daily sitting time (minutes)	0.09 [-0.05;0.24]	0.15* [0.04;0.27]	0.10 [-0.07;0.27]	0.09 [-0.08;0.27]

Values are presented as regression coefficients [95% conf. interval]. Coefficients express the difference in each risk factor in dyad member 2 per unit difference in that same risk factor in dyad member one. *p<0.05. [1]Individuals with diagnosed diabetes were excluded. [2]Individuals with diagnosed hypertension were excluded. [3]In 15% of the dyads, one member did not complete the step test. [4]For spouses, height (cm) is used while for parents-offspring, grandparents-grandchildren and siblings, height-for-age is used and not adjusted for age-difference or sex.

Spouses were statistically significantly associated in systolic blood pressure and fitness status, while grandparent-grandchild dyads were only associated with regard to diastolic blood pressure. None of the four dyad types had a statically significant association for BMI.

Standardized regression coefficients are shown in Table 3. For spouses, parent-offspring and sibling dyads the standardized regression coefficients were highest for fitness status.

Table 3. Standardized regression coefficients for type 2 diabetes risk factors (adjusted for age-difference and sex)

	Spouses (91)	Parents-offspring (283)	Grandparents-grandchildren (97)	Siblings (148)
HbA1c[1]	0.19 [-0.11;0.50]	0.21* [0.02;0.40]	0.12 [-0.13;0.37]	0.26* [0.11;0.42]
Systolic Blood Pressure[2]	0.28* [0.01;0.54]	0.20* [0.08;0.33]	0.22 [-0.06;0.50]	0.20* [0.01;0.39]
Diastolic Blood pressure[2]	0.10 [-0.14;0.35]	0.02 [-0.11;0.15]	0.27* [0.03;0.05]	0.20* [0.01;0.39]
Height for age[4]	0.07 [-0.13;0.28]	0.26* [0.14;0.37]	0.08 [-0.13;0.31]	0.26* [0.09;0.42]
Body mass index	0.16 [-0.04;0.37]	0.02 [-0.11;0.16]	0.02 [-0.20;0.24]	0.14 [-0.03;0.31]
VO_2-max[3]	0.54* [0.32;0.76]	0.41* [0.28;0.54]	-0.09 [-0.38; 0.21]	0.41* [0.25;0.57]
Daily sitting time	0.11 [-0.09;0.31]	0.17* [0.04;0.32]	0.11 [-0.09;0.32]	0.09 [-0.10;0.27]

Values are presented as standardized regression coefficients [95% conf. interval]. *p<0.05

Concordance in risk factors

The results of the logistic regression models are shown in Table 4. At household level, effect estimates showed that if one member in the household had dysglycaemia, the OR of another household member having the same status was increased almost 20 times. Having diagnosed hypertension in the household increased the odds of another member having diagnosed or undiagnosed hypertension 2.6 times, whereas undiagnosed hypertension increased the odds of diagnosed or undiagnosed hypertension in another member 4.8 times. The ORs of being overweight or obese, underweight, unfit, smoker or former smoker were all statistically significantly higher if another member of the household had the same status as compared to if no one in the household had the same status (Table 4).

Table 4. Odds ratios of having a condition as a function of the disease or risk factor status in other members of the same household (adjusted for age, sex and household size)

Exposure (status	Outcome	Household level
Diagnosed diabetes	*Dysglycaemia*	0.8 [0.4; 2.0]
Dysglycaemia	*Dysglycaemia*	19.8 [11.0; 35.5]*
Diagnosed hypertension	*Diagnosed or undiagnosed hypertension*	2.6 [1.5; 4.5]*
Undiagnosed hypertension	*Diagnosed or undiagnosed hypertension*	4.8 [2.9; 8.0]*
Short stature	*Short stature*	10.9 [6.9; 17.0]*
Overweight or obesity	*Overweight or obesity*	9.0 [6.1; 13.2]*
Underweight	*Underweight*	13.7 [7.1; 26.3]*
Unfit	*Unfit*[5]	11.2 [7.4; 17.1]*
Smoker	*Smoker*	33.7 [15.8; 71.8]*
Former smoker	*Former smoker*	18.9 [9.4; 38.0]*

Values are presented as odds ratios [95% conf. interval]. *p<0.05. [1]Individuals with diagnosed diabetes were excluded. [2]Individuals with diagnosed hypertension were excluded. [3]In 15% of the dyads, one member did not complete the step test. [4]Not adjusted for age-difference. [5]Unfit is defined as a fitness level below middle derived from VO_2-max and grouped according to Astrand (1960).[34]

DISCUSSION

The results of the present study indicate that individuals living in the same household in rural Uganda share risk factors for T2D and cardio-metabolic diseases. We showed that, in particular for systolic blood pressure and fitness status, the spousal association was at least as strong as the association between siblings or parent-offspring pairs, indicating an effect of shared lifestyle behaviours. For other cardio-metabolic risk

factors the resemblance was more prominent between siblings and parent-offspring dyads, whereas grandparent-grandchild dyads were less alike.

To our knowledge this is the first study to investigate the resemblance of multiple cardio-metabolic risk factors in household clusters including several generations living and eating together on a daily basis. A German study of aerobic fitness found an ICC of 0.22 in fitness status in nuclear families, but no association when restricting the analyses to spouses.[35] Our findings of dyad resemblance in HbA1c, blood pressure, height and fitness status are in agreement with other epidemiological studies focusing on a single type of dyad[19, 20] or a single type of risk factor.[35,36] We are not aware of studies from low-income countries investigating household or dyad resemblance in risk factors for T2D.

Among the measured risk factors, fitness status had the highest ICC at household level and standardised regression coefficient among spouse, parent-offspring and sibling dyads. The high resemblance in fitness status is partly explained by the high heritability of VO_2-max.[21] However, in contrast to the German study[35] we also found a high association in spousal fitness status suggesting that also shared physical activity patterns may contribute to the high fitness status resemblance in our study population. In the Ugandan situation, a peasant's wife is most often also a peasant, and offspring help cultivating the family land. Shared daily activities as the explanation for spousal resemblance in fitness status is supported by a French study finding that spouses' physical activity patterns were only similar during weekend days.[37] In addition, walking was the primary means of transportation for most of the study participants, giving all individuals in the same household the same walking distance and elevation differential when e.g. going to the nearest trading centre. However, adjusting for elevation gave only a modest attenuation of the household ICC or the dyad resemblance in fitness status.

In line with the results of a meta-analysis,[38] spouses resembled each other with regard to systolic blood pressure. Contradicting other studies[10,38] we did not find a statistically significant spousal association for BMI, diastolic blood pressure or HbA1c. Discordance in ethnicity of spouses, low numbers of people living in the household and higher SES have previously been shown to attenuate the spousal association in BMI.[10] However, none of these factors were present or affected the absence of a spousal

BMI association on our study. Assortative mating and/or convergence over time are often used to explain spousal resemblance in risk factors for T2D.[12,39] However, studies of assortative mating and risk factors for T2D are almost exclusively from high-income settings, and preferences for choice of spouse may differ across geographical, social and ethnic settings. For instance, overweight has traditionally been viewed as a desirable feature in SSA settings[40] whereas it is more stigmatizing in high-income settings.[41] Further, until recently the prevalence of obesity in SSA was low, and results from a Danish study showed a tendency to an increase in assorted marriages between obese spouses along with the obesity epidemic.[39]

In contrast to other studies of genetically related individuals, we did not find a relationship in BMI for parent-offspring[18,42] or sibling dyads.[19,36,43] Concerning parent-offspring, a study from the U.S including children from 2-16 years of age suggested that pubertal children are less likely to resemble their parents in BMI than pre-puberty children, as they grow more independent of parents' eating and exercise behaviours.[42] This could explain the lack of parent-offspring relationship in our study where some of the parent-offspring dyads included adult offspring. However, stratifying parent-offspring dyads into adolescents and adult offspring or above/below median age-difference did not change the lack of statistical associations. In terms of siblings, other studies found that sibling dyads resembled in BMI,[19] but that the sibling BMI correlations were less pronounced during adolescence,[36] decreased with increasing age difference[19] and were higher among home living adolescents than adult siblings living apart.[43] The mean sibling age difference (7 years) in our study was not markedly different from the mentioned studies, and the siblings lived together. Thus, these factors cannot entirely explain the lack of relationship.

The last relationship with a genetic component examined in the present study was grandparent-grandchild dyads. Again no relationship was seen in BMI, which is supported by data from a Korean population,[44] but in contrast to a study from Belgium finding a direct association in obesity measures through three generations.[45] Neither the Korean nor the Belgian study reported that grandparents and grandchildren lived together, which they did in our study and could have increased the chance of resemblance in BMI. However, Uganda is a country in transition in terms of both disease burden and nutrition. In addition, the Ruwenzori Mountain region in Kasese district was the centre of civil strife with a

civil war in 1962-1982 and again from 1996-2002, making it likely that grandparents and grandchildren were exposed to very different intrauterine environments and growth conditions. This hypothesis is supported by the findings of a statistically significant height increment between each of the three generations in our cohort (data not shown), which was not reported in the study from Korea including three generations.[44] Potential unmeasured confounders for BMI may have been unreported/undiagnosed infectious disease such as tuberculosis or HIV/AIDS; both have a fairly high prevalence in the study setting[46] and both affect body weight.

The high ORs in smoking status may partly be explained by a low overall smoking prevalence (7.6%). Further, 63% of the smokers lived together with at least one other smoker. The high resemblance in smoking status is supported by results of studies finding a high spousal resemblance in smoking status[12] and that both smoking and quitting smoking spread in social ties in social networks.[47]

Strengths and limitations

One of the main strengths of this study is the household-based approach. Visiting the families in the home setting resulted in a high individual response rate (97.5%) and thus only minimal risk of selection bias in dyad representativeness. The cross-sectional design prevents us from concluding on whether the spousal resemblance was due to shared risk behaviours or assortative mating, and for the genetic relationships, we cannot distinguish between shared genes and shared environment/behaviours. The ICCs reflect the proportion of variances, whereby the sizes of the ICCs cannot be compared to other cohorts or settings. Thus, the size of ICCs should only be interpreted as a tool to investigate which risk factors resemble most strongly at the household level in the present cohort. The application of HbA1c as a diagnostic tool in African populations is debated [48]. However, in the present study, HbA1c was used to investigate resemblance in dyad members and not to diagnose diabetes. Due to the initial sampling of this study population, 50% of the households had a member with diagnosed T2D. We have previously shown that having diagnosed T2D in the household may have positive spill-over effects on the other members[22] potentially due to changes in diet and physical activity due to the diabetes status.[49] This could explain the difference between diagnosed T2D and dysglycaemia in the household as a risk factor for dysglycaemia in other members of the household.

CONCLUSION

The moderate to strong correlations in T2D risk factors at household level and between spouses, parent-offspring, and sibling dyads suggest that shared behavioural and environmental factors such as physical activity may influence the risk factor level among cohabiting individuals. The marked degree of household resemblance for certain T2D risk factors highlights the potential of the household setting for screening and prevention of T2D. Thus when one household member presents with elevated glucose, blood pressure, or physical inactivity, the entire household could benefit from lifestyle interventions.

Acknowledgement

We thank the people who opened their homes and took time to participate in this study, the field assistants for collecting data and carrying equipment up the mountain slopes, and the Kagando Hospital staff members for their hospitality and support. We also thank Dr. Adam Hulman, Department of Public Health, University of Aarhus, for help with data management and Soren Brage, University of Cambridge, for assistance with step-test data.

Author contribution statement

Dr. Jannie Nielsen developed the study protocol, collected the data, performed the statistical analyses and the interpretation of data, and drafted, revised and finalized the article.

Dr. Silver K. Bahendeka contributed to the protocol with substantial knowledge concerning diabetes in Uganda and specifically in Kasese district, took part in the later stage and final interpretation of data, and participated in developing, revising and finalizing the manuscript.

Professor Susan R. Whyte contributed to the development of the study protocol, took part in the later stage and final interpretation of data, and participated in developing, revising and finalizing the manuscript.

Associate Professor Dan W. Meyrowitsch contributed to the development of the study protocol, took part in the later stage and final interpretation of data, and participated in developing, revising and finalizing the manuscript.

Professor Ib C. Bygbjerg contributed to the development of the study protocol, took part in the later stage and final interpretation of data, and participated in developing, revising and finalizing the manuscript.

Professor Daniel R. Witte performed the statistical analysis and the interpretation of data, and participated in developing, revising and finalizing the manuscript.

Competing interests

Dr. Nielsen's PhD fellowship was partly funded by Novo Nordisk Fonden (grant no. 29847).

Funding

The study was sponsored by University of Copenhagen, Thorvald Madsens Fond, Aase and Ejnar Danielsens Fond, and Christian and Otilia Brorsons Rejselegat. No sponsor had any influence on the study design, data collection, analysis, or interpretation or the writing of this article. The remaining authors have declared no conflict of interest.

Data sharing statement

No additional data available.

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STROBE CHECKLIST

Study: Household and familial resemblance in risk factors for type 2 diabetes and related cardio-metabolic diseases in rural Uganda

Type of study: Cross-sectional

	Item No	Recommendation	Page
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/ rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	5
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*6*
Bias	9	Describe any efforts to address potential sources of bias	5
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7
		(*b*) Describe any methods used to examine subgroups and interactions	7
		(*c*) Explain how missing data were addressed	6
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	9
		(b) Give reasons for non-participation at each stage	9
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8+9
		(b) Indicate number of participants with missing data for each variable of interest	9
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	10+11
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10+11
		(*b*) Report category boundaries when continuous variables were categorized	9
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	11
Discussion			
Key results	18	Summarise key results with reference to study objectives	12
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	13
Generalisability	21	Discuss the generalisability (external validity) of the study results	14+15
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	16

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.