JIDR Journal of Intellectual Disability Research
Published on behalf of mencap and in association with IASSID

Journal of Intellectual Disability Research doi: 10.1111/jir.13103

VOLUME 68 PART 3 pp 212–222 MARCH 2024

Obesity, diabetes and their metabolic correlates in middle-aged adults with Down syndrome

J. A. Luchsinger,[1,2] D. Pang,[3] S. J. Krinsky-McHale,[3] N. Schupf,[2,4,5] J. H. Lee,[2,4,5] W. Silverman[6] & W. B. Zigman[3]

1 *Department of Medicine, Columbia University Medical Center, New York, NY, USA*
2 *Department of Epidemiology, Columbia University Medical Center, New York, NY, USA*
3 *Department of Psychology, New York State Institute for Basic Research in Developmental Disabilities, New York, NY, USA*
4 *Gertrude H. Sergievsky Center, Columbia University Medical Center, New York, NY, USA*
5 *Taub Institute, Columbia University Medical Center, New York, NY, USA*
6 *Deparment of Pediatrics, University of California-Irvine, Irvine, CA, USA*

Abstract

Background Obesity in adults without Down syndrome is associated with an adverse metabolic profile including high prevalence of pre-diabetes and diabetes, high levels of insulin, non-high-density lipoprotein (HDL) cholesterol, leptin and high-sensitivity C-reactive protein (hsCRP) and low levels of HDL and adiponectin. We examined whether obesity in middle-aged adults with Down syndrome is also related to an adverse metabolic profile.

Methods This cross-sectional study included 143 adults with Down syndrome, with a mean age of 55.7 ± 5.7 years and 52.5% women. Body mass index (BMI) was classified as underweight (BMI < 18.5 kg/m^2), normal (BMI 18.5–24.9 kg/m^2), overweight (BMI 25–29.9 kg/m^2) and obese (BMI ≥ 30 kg/m^2). Diabetes was ascertained by history or by haemoglobin A1c (HbA1c) as normal glucose tolerance (HbA1c < 5.7%), pre-diabetes (HbA1c 5.7–6.4%) and diabetes (HbA1c ≥ 6.5%). We measured non-fasting lipids, hsCRP, insulin, adiponectin and leptin.

Results The majority of the sample had an overweight (46.9%) or obesity (27.3%) status. However, there was a relatively low prevalence of pre-diabetes (9.8%) and diabetes (6.9%). Overweight and obesity status were not associated with lower HDL and adiponectin and higher insulin, non-HDL cholesterol and hsCRP as expected in adults without Down syndrome. However, overweight and obesity were strongly associated with higher leptin ($P < 0.001$).

Conclusions The only metabolic correlate of obesity in middle-aged adults with Down syndrome was high leptin levels. Our findings are limited by non-fasting laboratory tests but suggest that middle-aged adults with Down syndrome do not have the adverse metabolic profile related to obesity found in adults without Down syndrome.

Keywords diabetes, Down syndrome, middle age, obesity

Correspondence: Dr José A. Luchsinger, Department of Medicine, Columbia University Medical Center, 630 West 168th Street, New York, NY 10032, USA (e-mail: jal94@cumc.columbia.edu).

© 2023 MENCAP and International Association of the Scientific Study of Intellectual and Developmental Disabilities and John Wiley & Sons Ltd.

Introduction

Down syndrome is defined cytogenetically by trisomy 21 and is the most common genetic cause of intellectual disability (ID), with a birth incidence of approximately 1/700 (Presson *et al.* 2013). Obesity is a commonly reported phenotypic feature of Down syndrome (Merrick & Shapira 2000), but estimates of prevalence have varied considerably for both younger subpopulations and adults. In addition, the consequences of obesity in middle-aged adults with Down syndrome are unclear. The survival of adults with Down syndrome has increased despite increased morbidity and mortality compared with the population without Down syndrome (Coppus *et al.* 2008; Irving *et al.* 2008; Zhu *et al.* 2013; Glasson *et al.* 2016). Thus, more persons with Down syndrome are surviving into middle and old age. In the population of adults without Down syndrome in the USA, this period of the lifespan is characterised by high prevalence of elevated adiposity (overweight and obesity) and type 2 diabetes and their metabolic correlates. Two-thirds of the US adult population suffers from pre-diabetes and type 2 diabetes (Centers for Disease Control and Prevention; http://www.cdc.gov//diabetes/pubs/factsheet11.htm), paralleling the similarly high prevalence for overweight and obesity (Hales *et al.* 2020). There is a paucity of information on these common conditions in middle-aged and older adults with Down syndrome. Thus, we sought to examine the prevalence of elevated adiposity and pre-diabetes and diabetes in middle-aged adults with Down syndrome and describe their metabolic correlates, including lipids, glycaemia, inflammation, insulin and adipokines (leptin and adiponectin), in an ongoing study of Down syndrome and aging (Silverman *et al.* 2004).

Methods

Design

The current report is from a cross-sectional analysis of an ongoing cohort study of adults with Down syndrome funded by the National Institutes of Health in the USA (Schupf *et al.* 2015). This longitudinal study employs a cross-sequential research design, with longitudinal testing of adults with Down syndrome, 45 years of age and older, evaluated up to three times, between October 2011 and December 2015. Evaluations included assessments of dementia status, together with a review of all medications and medical records at intervals ranging from 14 to 21 months. Maladaptive behaviour was measured using the Reiss Screen for Maladaptive Behavior (Havercamp & Reiss 1997) to provide information on depression, psychosis and other changes that might mimic or are associated with dementia (Urv *et al.* 2008), the primary outcome of the parent cohort study of Down syndrome. Cognitive abilities were assessed using a battery that covered a wide range of ID. Blood samples for determination of Down syndrome karyotype and various metabolic correlates were collected from willing subjects via non-fasting venipuncture by qualified programme staff. This study has been approved by the Institutional Review Boards of the New York Institute for Basic Research in Intellectual Disabilities (Staten Island, New York), the New York Psychiatric Institute (Manhattan, New York) and the Johns Hopkins University School of Medicine (Baltimore, Maryland). A full description of the instrument battery and study procedures has been previously published (Silverman *et al.* 2004). The current study presents results from a cross-sectional analysis of data from the first wave of data collection.

Participants and recruitment

The sample was composed of adults with Down syndrome receiving services from social service agencies in the New York State and the greater New York City metropolitan area in the USA who were 45 years of age or older. Once interest of potential participants was established by personnel of agencies providing their direct services, study materials were provided and consent/assent was obtained consistent with Institutional Review Board-approved procedures. All volunteers had the option of declining to participate in any component of the evaluations at any time, even when informed consent had been provided previously. Valid consents were received for 191 participants; however, we were only able to obtain blood samples from 143 participants (73.9%), primarily due to participant disinclination to undergo phlebotomy. Fasting was not required prior to phlebotomy. The current analyses are based on these baseline results. Formal evaluations completed included (1) clinical record reviews, (2) staff interviews, (3) cognitive assessments, (4) physical

© 2023 MENCAP and International Association of the Scientific Study of Intellectual and Developmental Disabilities and John Wiley & Sons Ltd.

13652788, 2024, 3, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/jir.13103 by Columbia University Libraries, Wiley Online Library on [13/01/2026]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

measurements/neurological evaluations and (5) collection of random blood samples. Our neurocognitive assessment battery was designed to assess domains of cognition and behaviour that are typically affected in Alzheimer's dementia, which persons with Down syndrome are at high risk of, and was tailored for use with adults having ID, as previously described (Silverman *et al.* 2004). Classification of dementia status was determined at consensus conferences using all available performance data. Participants were considered to have dementia if there was a history of progressive memory loss, disorientation and functional decline over a period of at least 1 year and if no medical or psychiatric conditions that might mimic dementia were present. Participants were classified as not having dementia if they were without cognitive or functional decline or if they showed only mild declines of insufficient severity to meet criteria for dementia.

Variables

The main exposure variable was body mass index (BMI) calculated as weight in kilograms divided by height in metres squared. BMI was categorised as underweight (BMI < 18.5 kg/m^2), normal (BMI 18.5–24.9 kg/m^2), overweight (BMI 25–29.9 kg/m^2) and obese (BMI ≥ 30 kg/m^2), following the World Health Organization criteria (Heiat *et al.* 2001). Diabetes categories were normal glucose tolerance (NGT), pre-diabetes and diabetes, following the American Diabetes Association guidelines (American Diabetes Association Professional Practice 2022). NGT was defined as haemoglobin A1c (HbA1c) of $<5.7\%$, and pre-diabetes was defined by an HbA1c between 5.7% and 6.4%. Diabetes was defined by history of type 1 or type 2 diabetes or an HbA1c of $\geq 6.5\%$.

Metabolic correlates that were examined included lipids, insulin, adiponectin, leptin and high-sensitivity C-reactive protein (hsCRP). Low-density lipoprotein (LDL) was calculated with the formula total cholesterol − (triglycerides/5) − high-density lipoprotein (HDL) (Friedewald *et al.* 1972). Non-HDL cholesterol was calculated as total cholesterol − HDL. Lipid profile (HDL, triglycerides and cholesterol) and hsCRP in human serum were measured using Cobas Integra 400 plus analyser (Roche Diagnostics, Indianapolis, USA) together with quality controls at high and low levels. HbA1c in whole blood was quantified by a turbidimetric inhibition immunoassay on Cobas Integra 400 plus analyser (Roche Diagnostics). Adiponectin and leptin were measured with radioimmunoassay (EMD Millipore Corporation, Billerica, MA, USA). Insulin was also measured with radioimmunoassay (Siemens Healthcare Diagnostics, Tarrytown, NY, USA). Given the polypharmacy common in persons with Down syndrome, we ascertained the following medication categories: thyroxine supplements, hypertension medications (angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, beta-blockers, calcium channel blockers and diuretics), diabetes medications (metformin, sulfonylurea, insulin, thiazolidinediones and glucagon-like peptide 1 agonists), lipid medications (hydroxymethylglutaryl-CoA reductase inhibitors and fibrates) and psychiatric medications (selective serotonin reactive inhibitors, antipsychotics, serotonin–norepinephrine reuptake inhibitors and norepinephrine–dopamine reuptake inhibitors). The rationale for including these medications is that they may affect some of the metabolic variables in the analyses. Use of lipid-lowering medications was expected to be related to lower non-HDL cholesterol level. Use of diabetes medications could affect adipokines and HbA1c. Use of psychiatric medications could be associated with weight gain and higher BMI (Berkowitz & Fabricatore 2011). Use of thyroxine could affect weight and obesity status. We lacked blood pressure measurements, and use of hypertension medication was used as an indicator of hypertension history. Other variables examined because they are common correlates of Down syndrome included severity of ID (operationalised as intellectual quotient), history of hypothyroidism (Hardy *et al.* 2004), history of hyperlipidaemia (Zigman *et al.* 2007) and presence of dementia (Zigman *et al.* 2007).

Statistical analysis

Distributions of all variables were examined. Insulin, leptin and hsCRP required natural logarithmic transformation to achieve a normal distribution. We examined Pearson's correlations among continuous variables. We compared characteristics across

© 2023 MENCAP and International Association of the Scientific Study of Intellectual and Developmental Disabilities and John Wiley & Sons Ltd.

13652788, 2024, 3, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/jir.13103 by Columbia University Libraries, Wiley Online Library on [13/01/2026]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

categories of adiposity and diabetes using analysis of variance for continuous variables and chi-squared for categorical variables. We conducted multivariate analyses relating exposure categories to continuous variables using analysis of covariance. All analyses were performed using SAS 9.3.

Results

Out of a total of 191 participants examined, 143 (74.87%) underwent phlebotomy and comprise the analytic sample. There were no statistically significant differences between those who underwent phlebotomy and those who did not in age, gender, ethnic and racial group, intellectual quotient, dementia prevalence, history of diabetes, history of dyslipidaemia and BMI (Table S1). Table 1 shows the general characteristics of the analytic sample. The mean age was 55.7 ± 5.7 years, 52.5% were women and 93.5% were Non-Hispanic White. The majority of the sample was categorised as having overweight (46.9%) or obesity (27.3%), but only 9.8% had pre-diabetes and 6.9% had diabetes. A total of 10 participants had diabetes, of which 2 were diagnosed as type 1 diabetes and 8 as type 2 diabetes.

Table 2 shows the correlation among continuous variables. BMI was modestly directly correlated with HbA1c and hsCRP and was moderately correlated with leptin. HbA1c was modestly directly correlated with hsCRP and insulin. Total cholesterol was moderately correlated with triglycerides and HDL and strongly correlated with LDL and non-HDL cholesterol. Triglycerides were modestly inversely correlated with HDL and adiponectin, modestly directly correlated with LDL and moderately correlated with non-HDL cholesterol. HDL was modestly correlated with adiponectin. LDL was strongly correlated with non-HDL cholesterol. hsCRP was modestly correlated with leptin. Insulin was modestly correlated with leptin.

We examined the relation of medication use with metabolic parameters (Table S2). Thyroxine supplement use was related to higher adiponectin levels ($P = 0.003$). Use of lipid medications was related to higher HbA1c ($P = 0.003$) and lower non-HDL cholesterol ($P = 0.0009$). Use of hypertension medications was related to higher HbA1c ($P = 0.04$) and higher hsCRP ($P = 0.004$).

Table 1 Characteristics of the cohort of 143 persons with Down syndrome at the time of assessments

Characteristic	Value
Sample size	143
Age in years	55.7 ± 5.7
Women	75 (52.5)
Non-Hispanic White	130 (93.5)
Intellectual quotient	36.9 ± 7.5
Dementia diagnosis	13 (9.1)
Type 1 diabetes history	2 (1.4)
Type 2 diabetes history	9 (6.3)
Dyslipidaemia history	57 (39.9)
Hypothyroidism history	87 (60.8)
Thyroxine supplements	72 (50.4)
Lipid medications	54 (37.4)
Hypertension medications	18 (12.6)
Diabetes medications	8 (5.6)
Psychiatric medications	58 (40.6)
Body mass index in kg/m^2 ± SD	28.3 ± 5.3
Body mass index (BMI) category	
Underweight (BMI $<$ 18.5 kg/m^2)	6 (4.1)
Normal (BMI 18.5–24.9 kg/m^2)	31 (21.7)
Overweight (BMI 25–29.9 kg/m^2)	67 (46.9)
Obese (BMI $\geq$ 30 kg/m^2)	39 (27.3)
Haemoglobin A1c (HbA1c) in % [mmol/mol]	5.5 ± 0.5 [37 ± 3.1]
Diabetes categories	
Normal glucose tolerance (HbA1c $<$ 5.7%)	119 (83.2)
Pre-diabetes (HbA1c 5.7–6.4%)	14 (9.8)
Diabetes (HbA1c $\geq$ 6.5%)	10 (6.9)
Total cholesterol in mg/dL	162.3 ± 31.4
High-density lipoprotein (HDL) in mg/dL	51.1 ± 11.4
Triglycerides in mg/dL	1175 ± 50.1
Low-density lipoprotein in mg/dL	87.7 ± 25.1
Non-HDL cholesterol in mg/dL	111.2 ± 29.5
High-sensitivity C-reactive protein (hsCRP) in mg/L	7.5 ± 15.2
hsCRP median (interquartile range) in mg/L	3.2 (1.4–6.5)
Insulin in IU/dL	25.4 ± 18.4
Insulin median (interquartile range) in IU/dL	19.7 (11.9–30.8)
Leptin in ng/mL	21.9 ± 27.8
Leptin median (interquartile range) in ng/mL	13.4 (6.6–26.2)
Adiponectin in ng/mL	17 678.6 ± 9197.6

Continuous variables are presented as means ± standard deviations. Categorical variables are presented as frequencies (percentages). For variables not normally distributed, both means ± standard deviations and medians (interquartile ranges) are presented.

Use of diabetes medications was related to higher HbA1c ($P < 0.0001$), lower non-HDL cholesterol ($P = 0.0008$) and lower hsCRP ($P = 0.01$). Use of psychiatric medications was not related to any metabolic parameter.

© 2023 MENCAP and International Association of the Scientific Study of Intellectual and Developmental Disabilities and John Wiley & Sons Ltd.

13652788, 2024, 3, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/jir.13103 by Columbia University Libraries, Wiley Online Library on [13/01/2026]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2 Pearson's correlation coefficients for continuous variables

	Age	IQ	BMI	HbA1c	TC	Trig	HDL	LDL	NHC	hsCRP	INS	LEP	ADI
Age	1	−0.2	−0.1	0.0	−0.1	−0.1	0.2	−0.1	−0.1	0.2	0.0	−0.1	0.1
		0.02	*0.26*	*0.97*	*0.47*	*0.02*	*0.02*	*0.15*	*0.10*	*0.008*	*0.94*	*0.94*	*0.33*
Intellectual quotient (IQ)		1.0	0.0	0.0	−0.1	0.0	0.0	−0.1	−0.1	0.0	0.2	0.0	−0.1
			0.69	*0.99*	*0.47*	*0.86*	*0.78*	*0.35*	*0.38*	*0.61*	*0.07*	*0.99*	*0.54*
Body mass index (BMI)			1.0	0.2	−0.1	0.07	−0.08	−0.1	−0.09	0.2	0.09	0.6	−0.1
				0.01	*0.69*	*0.38*	*0.31*	*0.09*	*0.27*	*0.02*	*0.40*	*<0.0001*	*0.26*
Haemoglobin A1c (HbA1c)				1.0	−0.1	−0.0	0.1	−0.1	−0.1	0.2	0.3	0.2	0.1
					0.26	*0.69*	*0.42*	*0.10*	*0.13*	*0.008*	*0.01*	*0.06*	*0.13*
Total cholesterol (TC)					1.0	0.4	0.3	0.9	0.9	−0.2	0.1	0.1	−0.0
						<0.0001	*<0.0001*	*<0.0001*	*<0.0001*	*0.05*	*0.65*	*0.28*	*0.82*
Triglycerides (Trig)						1.0	−0.3	0.3	0.6	−0.1	0.0	0.0	−0.4
							<0.0001	*0.0005*	*<0.0001*	*0.15*	*0.71*	*0.57*	*<0.0001*
High-density lipoprotein (HDL)							1.0	0.1	−0.0	−0.1	0.1	0.0	0.3
								0.19	*0.80*	*0.42*	*0.25*	*0.69*	*0.002*
Low-density lipoprotein (LDL)								1.0	0.9	−0.1	0.0	0.1	0.0
									<0.0001	*0.12*	*0.89*	*0.32*	*0.82*
Non-HDL cholesterol (NHC)									1.0	−0.1	0.00	0.1	0.0
										0.07	*0.99*	*0.35*	*0.82*
High-sensitivity C-reactive protein (hsCRP) natural log transformed										1.0	0.2	0.3	0.0
											0.07	*0.0006*	*0.58*
Insulin (INS) natural log transformed											1.0	0.2	0.1
												0.05	*0.26*
Leptin (LEP) natural log transformed												1.0	0.0
													0.71
Adiponectin (ADI)													1.0

P values are presented in italics. Logarithmically transformed values were used for variables that were not normally distributed, including high-sensitivity C-reactive protein, insulin and leptin.

Table 3 shows the comparison of characteristics among BMI categories. The only significant differences were for sex (women prevalence increased with higher BMI category), pre-diabetes (higher in the overweight and obese categories) and leptin, which showed a graded increase with higher BMI categories. The dose–response association of BMI category with leptin remained after adjustment for demographics and medication use ($P < 0.0001$). The means and standard deviations for logarithmically transformed leptin were 1.8 ± 0.8 for underweight, 1.9 ± 0.8 for normal, 2.5 ± 0.8 for overweight and 3.3 ± 0.9 for obesity.

The proportion of persons with NGT was lower in the overweight and obese categories, and this association was close to statistical significance. Persons with normal BMI did not have pre-diabetes, as compared with other BMI categories. BMI category was not associated with diabetes, lipids, hsCRP or adiponectin.

Table 4 shows the comparison of characteristics among diabetes categories. As expected, a history of hyperlipidaemia was higher in persons with pre-diabetes and diabetes. The prevalence of dementia was higher in persons with pre-diabetes. However, this observation is limited by the low number of cases of dementia and should be interpreted with caution. LDL and non-HDL cholesterol were appreciably lower in persons with diabetes. hsCRP showed a graded increase with diabetes categories. Insulin was higher in persons with pre-diabetes and diabetes. Leptin and adiponectin were not associated with diabetes categories.

© 2023 MENCAP and International Association of the Scientific Study of Intellectual and Developmental Disabilities and John Wiley & Sons Ltd.

13652788, 2024, 3, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/jir.13103 by Columbia University Libraries, Wiley Online Library on [13/01/2026]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3 Comparison of demographic and metabolic characteristics across body mass index (BMI) groups

Characteristic	Underweight (BMI < 18.5 kg/m^2)	Normal (BMI 18.5–24.9 kg/m^2)	Overweight (BMI 25–29.9 kg/m^2)	Obese (BMI ≥ 30 kg/m^2)	*P* value
Sample size	6	31	67	39	
Age in years	53.2 ± 2.6	56.2 ± 6.2	56.4 ± 5.6	55.4 ± 5.4	0.45
Women	2 (33.3)	14 (45.2)	31 (46.3)	28 (71.8)	0.03
Type 1 diabetes history	0	0	1 (1.49)	1 (2.56)	0.82
Type 2 diabetes history	0	1 (3.2)	3 (4.5)	5 (12.8)	0.25
Hyperlipidaemia	2 (33.3)	9 (29.0)	32 (47.8)	14 (35.9)	0.30
Thyroxine	1 (16.7)	17 (54.8)	35 (48.7)	19 (48.7)	0.37
Lipid medications	2 (33.3)	7 (22.6)	29 (43.3)	16 (41.0)	0.24
Hypertension medications	1 (16.7)	0 (0)	11 (16.4)	6 (15.4)	0.13
Diabetes medications	0 (0)	1 (3.2)	2 (2.9)	5 (12.8)	0.14
Psychiatric medications	2 (33.3)	14 (45.2)	24 (35.8)	18 (46.2)	0.67
Dementia	0.0	8 (17.4)	9 (11.1)	4 (6.9)	0.30
Hypothyroidism	2 (33.3)	18 (58.1)	43 (61.2)	24 (61.5)	0.50
HbA1c in % [mmol/mol]	5.4 ± 0.4 [36 ± 2.0]	5.3 ± 0.4 [34 ± 2.0]	5.4 ± 0.5 [36 ± 3.1]	5.6 ± 0.4 [38 ± 2.0]	0.16
Normal glucose tolerance	5 (83.3)	30 (96.8)	53 (79.1)	31 (79.4)	0.07
Pre-diabetes	1 (16.7)	0	10 (14.9)	3 (7.7)	0.03
Diabetes	0	1 (3.2)	4 (5.9)	5 (12.8)	0.32
Diabetes/pre-diabetes	1 (16.7)	1 (3.2)	14 (20.9)	8 (20.5)	0.11
Cholesterol in mg/dL	169.0 ± 43.5	167.5 ± 27.2	163.0 ± 35.2	155.8 ± 25.0	0.43
Triglycerides in mg/dL	117.8 ± 32.4	104.7 ± 38.4	125.2 ± 56.2	114.4 ± 48.5	0.29
High-density lipoprotein (HDL) in mg/dL	48.2 ± 8.8	53.9 ± 10.4	49.5 ± 10.8	51.9 ± 13.2	0.28
Low-density lipoprotein in mg/dL	97.3 ± 34.3	92.6 ± 23.2	88.5 ± 27.3	80.9 ± 19.5	0.18
Non-HDL cholesterol in mg/dL	120.8 ± 39.1	113.5 ± 28.4	113.5 ± 28.4	113.5 ± 32.5	0.31
hsCRP (log) in mg/L	0.9 ± 1.3	0.9 ± 1.3	1.1 ± 1.2	1.5 ± 1.2	0.20
Insulin (log) in IU/mL	3.9 ± 0.6	2.9 ± 0.5	2.9 ± 0.6	3.1 ± 0.7	0.41
Leptin (log) in ng/mL	1.9 ± 0.8	1.9 ± 0.8	2.5 ± 0.8	3.3 ± 0.9	<0.0001
Adiponectin in ng/mL	17 833.3 ± 6598.1	19 625.9 ± 7936.8	16 941.5 ± 9134.9	17 428.9 ± 10 552.2	0.63

Logarithmically transformed values are presented for variables that were not normally distributed, including high-sensitivity C-reactive protein (hsCRP), insulin and leptin. Continuous variables are presented as means ± standard deviations. Categorical variables are presented as frequencies (percentages). Continuous variables were compared with analysis of variance. Categorical variables were compared with chi-squared.

Discussion

We found that most middle-aged adults with Down syndrome had either overweight or obesity, replicating previous studies in persons with Down syndrome (Merrick & Shapira 2000; Melville *et al.* 2005) and similar to the population without Down syndrome in the USA (Hales *et al.* 2020). However, having overweight or obesity status was not accompanied by a high prevalence of pre-diabetes or diabetes comparable with the population without Down syndrome (Centers for Disease Control and Prevention; http://www.cdc.gov//diabetes/pubs/factsheet11.htm) in whom a third of adults 18 years and older has pre-diabetes or diabetes. The only strong correlate of BMI examined continuously and in clinically relevant BMI categories was leptin, which was higher with higher BMI, as expected. Higher BMI was not associated with insulin resistance, as evidenced by a lack of association with insulin and adiponectin levels. However, pre-diabetes and diabetes were associated with a higher history of dyslipidaemia, higher hsCRP and higher insulin levels, as expected, but were not associated with adiponectin and leptin levels. Lipid levels were lower in persons with pre-diabetes and diabetes, explained by treatment for the diagnosis of hyperlipidaemia, which was higher in persons with pre-diabetes and diabetes.

© 2023 MENCAP and International Association of the Scientific Study of Intellectual and Developmental Disabilities and John Wiley & Sons Ltd.

13652788, 2024, 3, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/jir.13103 by Columbia University Libraries, Wiley Online Library on [13/01/2026]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 4 Comparison of demographic and metabolic characteristics across diabetes groups [normal glucose tolerance (NGT), pre-diabetes and diabetes]

Characteristic	NGT	Pre-diabetes	Diabetes	*P* value
Sample size	119	14	10	
Age	55.5 ± 5.7	56.9 ± 6.1	56.1 ± 5.3	0.65
Women	63 (52.9)	7 (50.0)	5 (50.0)	0.96
Intellectual quotient	37.3 ± 7.9	33.8 ± 4.1	37.4 ± 6.1	0.32
HbA1c in % [mmol/mol]	5.3 ± 0.2 [34 ± 1.9]	5.7 ± 0.03 [39 ± 0.1]	1.6 ± 1.0 [34 ± 8.6]	<0.0001
Hyperlipidaemia history	42 (35.3)	7 (50.0)	8 (80.0)	0.01
Thyroxine supplements	56 (47.1)	8 (57.1)	8 (80.0)	0.12
Lipid medications	38 (31.9)	7 (50.0)	9 (90.0)	0.0008
Hypertension medications	12 (10.1)	1 (7.1)	5 (50.0)	0.001
Diabetes medications	0 (0.0)	0 (0.0)	8 (80.0)	<0.0001
Psychiatric medications	46 (38.7)	7 (50.0)	5 (50.0)	0.58
Dementia	8 (6.7)	5 (35.7)	0	0.001
Hypothyroidism	69 (57.9)	10 (71.4)	8 (80.0)	0.24
Body mass index in kg/m^2	28.0 ± 5.5	28.7 ± 2.7	30.6 ± 5.3	0.34
Total cholesterol in mg/dL	164.8 ± 31.7	156.4 ± 26.0	140.0 ± 28.5	0.05
Triglycerides in mg/dL	119.3 ± 50.3	122.1 ± 49.1	89.9 ± 45.0	0.19
High-density lipoprotein (HDL) in mg/dL	50.9 ± 11.2	50.3 ± 12.1	54.6 ± 12.9	0.59
Low-density lipoprotein in mg/dL	90.1 ± 24.9	81.6 ± 21.4	68.2 ± 22.9	0.01
Non-HDL cholesterol in mg/dL	113.9 ± 29.1	106.1 ± 26.7	86.2 ± 28.4	0.01
hsCRP (log) in mg/L	1.1 ± 1.1	1.5 ± 1.2	2.1 ± 1.4	0.01
Insulin (log) in IU/mL	2.9 ± 0.6	3.5 ± 0.7	3.4 ± 0.7	0.03
Leptin (log) in ng/mL	2.6 ± 0.9	2.9 ± 0.7	2.7 ± 1.3	0.33
Adiponectin in ng/mL	17 389.5 ± 8323.8	16 792.9 ± 9685.1	22 215.0 ± 16 036.9	0.26

Logarithmically transformed values are presented for variables that were not normally distributed, including high-sensitivity C-reactive protein (hsCRP), insulin and leptin. Continuous variables are presented as means ± standard deviations. Categorical variables are presented as frequencies (percentages). Continuous variables were compared with analysis of variance. Categorical variables were compared with chi-squared.

Our observations were not explained by differences in age, sex, severity of ID or co-morbid hypothyroidism, common in adults with Down syndrome (Hardy *et al.* 2004). It is possible that the modest association between obesity and the adverse metabolic correlates in persons with Down syndrome explains their reported low levels of atherosclerosis (Draheim *et al.* 2002; Corsi *et al.* 2009). However, we observed that hsCRP, a marker of higher cardiovascular risk (Ridker 2014), was higher in persons with pre-diabetes and diabetes and those using hypertension medications, suggesting that there may be subclinical cardiovascular disease in persons with Down syndrome with pre-diabetes and diabetes.

There is a paucity of data on clinically defined categories of obesity and diabetes status in middle-aged adults with Down syndrome. Our intent was to determine whether obesity observed in middle-aged adults with Down syndrome has the same adverse metabolic correlates as observed in the general population. A study from the UK (Melville *et al.* 2005) among 327 adults with Down syndrome aged 37.2 years found that 40% were obese and 44% were overweight, higher than in controls of similar age. A study from Spain (Real De Asua *et al.* 2014) among 51 persons with Down syndrome aged 36 years reported that 37% were overweight and 37% were obese. A study from the same group in Spain among 49 adults aged 36 years reported that while obesity was higher in persons with Down syndrome compared with controls, fasting insulin was higher, but glycaemia measured with HbA1c and cholesterol, triglycerides, HDL and LDL were similar. However, this study showed that persons with abdominal obesity, defined as a waist-to-height ratio of 0.5, had an unfavourable metabolic profile, including higher insulin, cholesterol, triglycerides and HDL, compared with those with lower abdominal obesity. This finding

© 2023 MENCAP and International Association of the Scientific Study of Intellectual and Developmental Disabilities and John Wiley & Sons Ltd.

13652788, 2024, 3, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/jir.13103 by Columbia University Libraries, Wiley Online Library on [13/01/2026]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

for abdominal obesity suggests that BMI may not be the best measure of adiposity in Down syndrome. Compared with these studies, our study similarly showed in an older population that the prevalence of overweight and obesity was high. However, higher adiposity ascertained by BMI was not related to worse insulin sensitivity as measured with random insulin and adiponectin and was related to a modestly higher risk of pre-diabetes compared with persons with normal BMI. The prevalence of overweight and obesity by BMI is similarly high in the general population but is accompanied by high prevalence of pre-diabetes and type 2 diabetes and an adverse metabolic profile that includes high insulin, cholesterol, triglycerides, LDL, hsCRP, leptin and low HDL and adiponectin. For example, a middle-aged cohort in New York City with a mean age of 59 years had a similar prevalence of overweight and obesity as in this study, but these conditions were accompanied by high prevalence of pre-diabetes (33%) and diabetes (30%) also defined by the American Diabetes Association guidelines using HbA1c and clinical history (Luchsinger *et al.* 2015).

The only strong expected correlate of BMI found in our sample was leptin, which was strongly correlated with BMI. There are few studies that have examined this association in persons with Down syndrome, mostly in children. An Egyptian study among 36 children with Down syndrome found that leptin was higher in those with obesity, similar to control children (Yahia *et al.* 2012). Another study from the USA of 35 children aged 6.6 years with Down syndrome reported that leptin was higher than in controls and that it was positively correlated with adiposity (Magge *et al.* 2008). An Italian study of eight women with Down syndrome reported a positive correlation of BMI and leptin. Corsi *et al.* (2009) reported that adults (20–50 years old) and elderly persons (>60 years old) with Down syndrome have higher leptin levels compared with controls without Down syndrome and that leptin levels seem to decrease with age among persons with Down syndrome. It seems that the relation of increased adiposity and leptin in persons with Down syndrome is similar to that of the population without Down syndrome. The implications of this observation are unclear. Leptin is a hormone that in low levels is a marker of starvation (Kmiec *et al.* 2005) and may have independent vascular consequences with high levels, such as increased blood pressure (Bell & Rahmouni 2016). Leptin has been hypothesised to be neuroprotective based on animal and epidemiologic data (Lieb *et al.* 2009), and this could explain the previously made observation that obesity in persons with Down syndrome is associated with better cognitive function (Patel *et al.* 2004). In the current analysis, the prevalence of dementia was appreciably lower in persons with obesity and overweight, but this association was not statistically significant.

We found no association between BMI and adiponectin. Corsi *et al.* (2009) reported that adiponectin levels are higher in persons with Down syndrome than in those without Down syndrome. Moreover, they reported that among persons with Down syndrome, those aged 60 years and older have higher adiponectin levels compared with those aged 20–50 years and that adiponectin levels are lowest in children aged 2–14 years. Their findings suggest that adiponectin levels increase with age in Down syndrome. It is possible that our middle-aged cohort had relatively homogeneous high levels of adiponectin, which could explain the lack of association with BMI. In addition, given that higher adiponectin is a marker of insulin sensitivity, it is possible that factors associated with higher adiponectin levels in middle-aged and older adults with Down syndrome could be a mechanism explaining the relatively low prevalence of pre-diabetes and diabetes that we observed.

We observed that dementia prevalence was higher in persons with pre-diabetes compared with those with NGT, but similar risk was not observed for persons with diabetes. This observation, although statistically significant, is limited by sparse data. The continuum of hyperglycaemia (including pre-diabetes and diabetes) in elderly persons in the general population is associated with increased dementia risk (Cheng *et al.* 2011). Thus, both pre-diabetes and diabetes are expected to be related to a higher dementia risk. However, type 2 diabetes in the general population is mostly due to insulin resistance caused by obesity (Festa *et al.* 2006), while diabetes in Down syndrome is due to insulin deficiency in most cases (Real De Asua *et al.* 2014). A minority of persons with Down syndrome may have hyperglycaemia in pre-diabetes through mechanisms similar to those in the general population (insulin resistance), and it is possible that this hyperglycaemia could cause

© 2023 MENCAP and International Association of the Scientific Study of Intellectual and Developmental Disabilities and John Wiley & Sons Ltd.

13652788, 2024, 3, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/jir.13103 by Columbia University Libraries, Wiley Online Library on [13/01/2026]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

dementia as in the general population. This possibility needs to be examined in larger samples and with longitudinal data. It is important to point out that the lifetime risk of dementia in Down syndrome is over 90% (Fortea *et al.* 2021), but the prevalence in our sample was only 9%. This discrepancy is likely explained by the relatively young age in our sample, and it is expected that the prevalence of dementia will increase exponentially as the cohort is followed. Continued follow-up will allow proper examination of the association between metabolic factors and dementia risk.

The main strength of our study is that it examined the metabolic correlates of adiposity in a relatively large sample of middle-aged persons with Down syndrome compared with previous studies in smaller samples and mostly younger cohorts. However, our study has several limitations. We did not have a comparison group of persons without Down syndrome and relied on published data in the general population for comparisons. We did not have blood pressure data to examine this important correlate of obesity and diabetes. This precluded us from examining hypertension and the metabolic syndrome, which have been reported to be as prevalent in persons with ID as in the general population (De Winter *et al.* 2011). In addition, fasting phlebotomy was not required and the levels of measures that are dependent on fasting (triglycerides, insulin and leptin) should be interpreted as random levels. Measurement error in non-fasting assays of triglycerides, insulin and leptin could have led to regression dilution bias (bias towards null findings) and could explain the lack of association between BMI status and insulin in our sample. The measurements of adiponectin, HbA1c, hsCRP, HDL and non-HDL cholesterol are less sensitive to fasting status and our results for these measures seem unlikely to be biased by measurement error. We also could not properly assess insulin resistance though measures like the Homeostatic Model Assessment for Insulin Resistance because we lacked fasting glucose and insulin. We lacked measures of central obesity such as waist-to-height ratio, which is better correlated with insulin resistance compared with BMI (Real De Asua *et al.* 2014). Thus, it is possible that our null findings could be explained by the use of BMI as the measure of adiposity rather than measures of abdominal obesity. Lastly, although we examined medications as covariates, we lacked data on dosing and duration and could not properly account for this confounder.

While middle-aged persons with Down syndrome have a high prevalence of overweight and obesity similar to the general population, this high prevalence of overweight and obesity is not accompanied by the adverse metabolic profile observed in the population of adults without Down syndrome, with the exception of high levels of leptin. The implications of this observation for the health and well-being for this rapidly growing aged population need to be understood and could provide insights into protective factors for the general population at risk for type 2 diabetes. Factors associated with high adiponectin in adults with Down syndrome could explain the lack of association of higher BMI with an adverse metabolic profile and could be targeted for further research.

Author contributions

J. A. Luchsinger and W. B. Zigman were responsible for study conception, data analyses and drafting of the manuscript. D. Pang was responsible for data collection and drafting of the manuscript. S. J. Krinsky-McHale, N. Schupf, J. H. Lee, W. Silverman and W. B. Zigman were responsible for the parent study conception, funding and drafting of the manuscript. J. A. Luchsinger is the guarantor of the manuscript.

Acknowledgements

The investigators are grateful to the study participants, their families and the agencies that provide them with services.

Source of funding

The primary support for this project was provided by the Eunice Kennedy Shriver National Institute of Child Health and Human Development (grant P01HD035897). This project was also partially supported by the National Center for Advancing Translational Sciences (grant 1UL1TR001873, previously 1U54TR001633) and the National Institutes of Health (grant K24AG045334).

© 2023 MENCAP and International Association of the Scientific Study of Intellectual and Developmental Disabilities and John Wiley & Sons Ltd.

13652788, 2024, 3, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/jir.13103 by Columbia University Libraries, Wiley Online Library on [13/01/2026]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conflict of interest

None to report.

Ethics approval statement

This study has been approved by the Institutional Review Boards of the New York Institute for Basic Research in Intellectual Disabilities (Staten Island, New York), the New York Psychiatric Institute (Manhattan, New York) and the Johns Hopkins University School of Medicine (Baltimore, Maryland).

Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

References

American Diabetes Association Professional Practice, C (2022) 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes – 2022. *Diabetes Care* **45**, S17–38.

Bell B. B. & Rahmouni K. (2016) Leptin as a mediator of obesity-induced hypertension. *Current Obesity Reports* **5**, 397–404.

Berkowitz R. I. & Fabricatore A. N. (2011) Obesity, psychiatric status, and psychiatric medications. *The Psychiatric Clinics of North America* **34**, 747–64.

Cheng D., Noble J., Tang M. X., Schupf N., Mayeux R. & Luchsinger J. A. (2011) Type 2 diabetes and late-onset Alzheimer's disease. *Dementia and Geriatric Cognitive Disorders* **31**, 424–30.

Coppus A. M., Evenhuis H. M., Verberne G. J., Visser F. E., Oostra B. A., Eikelenboom P. *et al.* (2008) Survival in elderly persons with Down syndrome. *Journal of the American Geriatrics Society* **56**, 2311–6.

Corsi M. M., Dogliotti G., Pedroni F., Galliera E., Malavazos A. E., Villa R. *et al.* (2009) Adipocytokines in Down's syndrome, an atheroma-free model: role of adiponectin. *Archives of Gerontology and Geriatrics* **48**, 106–9.

De Winter C. F., Magilsen K. W., Van Alfen J. C., Willemsen S. P. & Evenhuis H. M. (2011) Metabolic syndrome in 25% of older people with intellectual disability. *Family Practice* **28**, 141–4.

Draheim C. C., McCubbin J. A. & Williams D. P. (2002) Differences in cardiovascular disease risk between nondiabetic adults with mental retardation with and without Down syndrome. *American Journal of Mental Retardation* **107**, 201–11.

Festa A., Williams K., D'agostino R., Jr., Wagenknecht L. E. & Haffner S. M. (2006) The natural course of β-cell function in nondiabetic and diabetic individuals: the Insulin Resistance Atherosclerosis Study. *Diabetes* **55**, 1114–20.

Fortea J., Zaman S. H., Hartley S., Rafii M. S., Head E. & Carmona-Iragui M. (2021) Alzheimer's disease associated with Down syndrome: a genetic form of dementia. *Lancet Neurology* **20**, 930–42.

Friedewald W. T., Levy R. I. & Fredrickson D. S. (1972) Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clinical Chemistry* **18**, 499–502.

Glasson E. J., Jacques A., Wong K., Bourke J. & Leonard H. (2016) Improved survival in Down syndrome over the last 60 years and the impact of perinatal factors in recent decades. *The Journal of Pediatrics* **169**, 214–20 e1.

Hales C. M., Carroll M. D., Fryar C. D. & Ogden C. L. (2020) Prevalence of obesity and severe obesity among adults: United States, 2017–2018. *NCHS Data Brief*, 1–8.

Hardy O., Worley G., Lee M. M., Chaing S., Mackey J., Crissman B. *et al.* (2004) Hypothyroidism in Down syndrome: screening guidelines and testing methodology. *American Journal of Medical Genetics. Part A* **124A**, 436–7.

Havercamp S. M. & Reiss S. (1997) The Reiss Screen for Maladaptive Behavior: confirmatory factor analysis. *Behaviour Research and Therapy* **35**, 967–71.

Heiat A., Vaccarino V. & Krumholz H. M. (2001) An evidence-based assessment of federal guidelines for overweight and obesity as they apply to elderly persons. *Archives of Internal Medicine* **161**, 1194–203.

Irving C., Basu A., Richmond S., Burn J. & Wren C. (2008) Twenty-year trends in prevalence and survival of Down syndrome. *European Journal of Human Genetics* **16**, 1336–40.

Kmiec Z., Pokrywka L., Kotlarz G., Kubasik J., Szutowicz A. & Mysliwski A. (2005) Effects of fasting and refeeding on serum leptin, adiponectin and free fatty acid concentrations in young and old male rats. *Gerontology* **51**, 357–62.

Lieb W., Beiser A. S., Vasan R. S., Tan Z. S., Au R., Harris T. B. *et al.* (2009) Association of plasma leptin levels with incident Alzheimer disease and MRI measures of brain aging. *JAMA* **302**, 2565–72.

Luchsinger J. A., Cabral R., Eimicke J. P., Manly J. J. & Teresi J. (2015) Glycemia, diabetes status, and cognition in Hispanic adults aged 55–64 years. *Psychosomatic Medicine* **77**, 653–63.

Magge S. N., O'neill K. L., Shults J., Stallings V. A. & Stettler N. (2008) Leptin levels among prepubertal children with Down syndrome compared with their siblings. *The Journal of Pediatrics* **152**, 321–6.

© 2023 MENCAP and International Association of the Scientific Study of Intellectual and Developmental Disabilities and John Wiley & Sons Ltd.

13652788, 2024, 3, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/jir.13103 by Columbia University Libraries, Wiley Online Library on [13/01/2026]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Melville C. A., Cooper S. A., McGrother C. W., Thorp C. F. & Collacott R. (2005) Obesity in adults with Down syndrome: a case-control study. *Journal of Intellectual Disability Research* **49**, 125–33.

Merrick J. & Shapira J. (2000) Obesity in persons with Down syndrome. *International Journal of Adolescent Medicine and Health* **12**, 69–74.

Patel B. N., Pang D., Stern Y., Silverman W., Kline J. K., Mayeux R. *et al.* (2004) Obesity enhances verbal memory in postmenopausal women with Down syndrome. *Neurobiology of Aging* **25**, 159–66.

Presson A. P., Partyka G., Jensen K. M., Devine O. J., Rasmussen S. A., McCabe L. L. *et al.* (2013) Current estimate of Down syndrome population prevalence in the United States. *The Journal of Pediatrics* **163**, 1163–8.

Real De Asua D., Parra P., Costa R., Moldenhauer F. & Suarez C. (2014) A cross-sectional study of the phenotypes of obesity and insulin resistance in adults with Down syndrome. *Diabetes and Metabolism Journal* **38**, 464–71.

Ridker P. M. (2014) Inflammation, C-reactive protein, and cardiovascular disease: moving past the marker versus mediator debate. *Circulation Research* **114**, 594–5.

Schupf N., Lee A., Park N., Dang L. H., Pang D., Yale A. *et al.* (2015) Candidate genes for Alzheimer's disease are associated with individual differences in plasma levels of beta amyloid peptides in adults with Down syndrome. *Neurobiology of Aging* **36**, e1–0.

Silverman W., Schupf N., Zigman W., Devenny D., Miezejeski C., Schubert R. *et al.* (2004) Dementia in adults with mental retardation: assessment at a single point in time. *American Journal of Mental Retardation* **109**, 111–25.

Urv T. K., Zigman W. B. & Silverman W. (2008) Maladaptive behaviors related to dementia status in adults with Down syndrome. *American Journal of Mental Retardation* **113**, 73–86.

Yahia S., El-Farahaty R. M., El-Hawary A. K., El-Hussiny M. A., Abdel-Maseih H., El-Dahtory F. *et al.* (2012) Leptin, insulin and thyroid hormones in a cohort of Egyptian obese Down syndrome children: a comparative study. *BMC Endocrine Disorders* **12**, 22.

Zhu J. L., Hasle H., Correa A., Schendel D., Friedman J. M., Olsen J. *et al.* (2013) Survival among people with Down syndrome: a nationwide population-based study in Denmark. *Genetics in Medicine* **15**, 64–9.

Zigman W. B., Schupf N., Jenkins E. C., Urv T. K., Tycko B. & Silverman W. (2007) Cholesterol level, statin use and Alzheimer's disease in adults with Down syndrome. *Neuroscience Letters* **416**, 279–84.

Accepted 11 October 2023

Supporting Information

Additional Supporting Information may be found online in the supporting information tab for this article.

Table S1. Comparison between participants with phlebotomy included in the analyses and those excluded who did not undergo phlebotomy. Continuous variables are presented as means ± standard deviations. Categorical variables are presented as frequencies (percentages). Continuous variables were compared with t-tests and categorical variables with chi-squared.

Table S2. Comparison of Hemoglobin A1c (HbA1c), High Density Lipoprotein (HDL), non-HDL Cholesterol, high sensitivity CRP (hsCRP), insulin, leptin, and adiponectin between persons taking and not taking thyroxine, lipid lowering medications, hypertension medications, diabetes medications, and psychiatric medications. Means ± Standard deviations and p values from t-tests are presented by the reported use of medication categories. hsCRP (lCRP), Insulin (linsulin) and leptin (lleptin) required logarithmic transformation.

© 2023 MENCAP and International Association of the Scientific Study of Intellectual and Developmental Disabilities and John Wiley & Sons Ltd.

13652788, 2024, 3, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/jir.13103 by Columbia University Libraries, Wiley Online Library on [13/01/2026]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License