

**Examining Association between Reported High Cholesterol and Risk Factors in Adults
with Intellectual and Developmental Disabilities: A Five Year Follow-Up**

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Having high cholesterol puts people at risk for heart disease, which is the leading cause of death in the United States (Arnett, Jacobs, Luepker, Blackburn, Armstrong, & Claas, 2005; Ford, Pearson, Zhao, & Mokdad, 2010; Hyre, Muntner, Menke, Raggi, & He, 2007; Kuklina, Yoon, & Keenan, 2010; Sinning, Leistner, & Landmesser, 2016; Williams, 2002). Heart disease is a term that includes coronary heart disease and other heart conditions that might affect the heart's muscle, valves or rhythm. According to the 1999-2006 National Health and Nutrition Examination Survey (NHANES) data, approximately 65% of young adults who had coronary heart disease (CHD) or a CHD equivalent as well as 26% of young adults who had 2 or more risk factor had a high low density lipoprotein (LDL) level (Kuklina, Yoon, & Keenan, 2010). Although mean total cholesterol, triglycerides, and LDL levels declined from 1999 to 2014 in the United States (Rosinger, Carroll, Lacher, & Ogden, 2017), high cholesterol remains a major risk factor for heart disease and stroke (Mayo Clinic, 2016; World Heart Federation, 2017). High cholesterol can cause atherosclerosis and reduced blood flow through the arteries which can contribute to CHD-related complications such as chest pain, heart attack and stroke (Mayo Clinic, 2016; World Heart Federation, 2017). Lowering cholesterol can reduce the risk of having a heart attack, needing heart bypass surgery or angioplasty, and dying of heart disease (CDC, 2011). Certain health conditions, lifestyles, and family history can increase an individual's risk for high cholesterol (CDC, 2016). For example, diabetes increases the risk for high cholesterol by causing sugars to build up in the blood due to insufficient insulin production or insulin resistance (Williams, 2002). Some of these risk factors are non-modifiable, such as age or family history; whereas, other risk factors such as diabetes, physical activity, diet and obesity are modifiable (Mayo Clinic, 2016). Not getting enough physical activity can contribute to weight gain. Obesity is linked to higher triglycerides, higher "bad" cholesterol levels, and lower

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"good" cholesterol levels. In addition to high cholesterol, obesity can also directly lead to heart disease, high blood pressure, and diabetes (CDC, 2016).

CHD is a substantial morbidity risk in older adults with IDD, hypertension, high cholesterol and diabetes mellitus directly related to CHD (de Winter, Magilsen, van Alfen, Penning, & Evenhuis, 2009; de Winter, Bastiaanse, Hilgenkamp, Evenhuis, & Echteld, 2012a; **Henderson, Robinson, Davidson, Haveman, Janicki, & Albertini, 2008**). Evidence also shows that adults with IDD are more likely to have high cholesterol than the general population and therefore a higher risk for CHD (**Henderson et al, 2008**; National University of Singapore, 2013; Sohler, Lubetkin, Levy, Soghomonian, & Rimmerman, 2009). The prevalence of some risk factors for high cholesterol is higher in adults with IDD than the general population. For instance, in comparison with the general population obesity is a significantly greater problem among adults with IDD (de Winter, Bastiaanse, Hilgenkamp, Evenhuis, & Echteld, 2012b; Hsieh, Rimmer, & Heller, 2014; Yamaki, 2005). People with IDD are at higher risk of diabetes which is attributed to obesity, reduced physical activity, elevated blood pressure, and poor nutrition (McVilly, McGillivray, Curtis, Lehmann, Morrish, & Speight, 2014; Rey-Conde, & Lennox, 2007; Rimmer & Yamaki, 2006). Prevalence rates of diabetes among people with IDD vary with studies suggesting occurrence rates between 0.4% to 25% (MacRae et al., 2015). According to de Winter and colleagues (2015), 12.5% of older people with IDD have diabetes compared to 9.1% of people in the general population. Reichard and Stolzle (2011) reported that 18.5% of people with IDD have diabetes compared to 3.7% of people in the general population with diabetes. Despite these different figures, overall studies have shown that people with autism (Cooper, Melville, & Morrison, 2004) and Down syndrome (Rimmer & Yamaki, 2006) have greater prevalence of diabetes than the general population. As such, it is imperative to study the

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effects of modifiable risk factors on high cholesterol in adults with IDD. However, there is very little empirical evidence, particularly from longitudinal studies, of the association between the aforementioned risk factors and high cholesterol among the IDD population. This study examined whether being physically inactive, having obesity, and/or having diabetes were predictors of reported high cholesterol over a 5 year span among adults with IDD. In addition, this study explored whether there were any mediating effects of diabetes on the relationship between obesity and high cholesterol.

Method

Participants

A total of 1,618 adults aged 18 years and older with IDD participated in the Longitudinal Health and Intellectual and Development Study (LHIDDS) over five years (4 time points: Year 1, 2, 3 & 5) and provided information regarding their health, physical function, and health behaviors. At Year 1 out of 2,841 surveys that were distributed, 1,618 surveys were completed and returned at baseline with an overall response rate of 57%. A total of 1,275 participants (79% response rate) completed the survey in Year 2, followed by 1,176 (76% response rate) in Year 3 and 924 (73% response rate) in Year 5. **The overall response rate of people who completed the first survey and returned data for each of the 4 years was 57% (n = 924).** The baseline cohort consisted of 726 females and 892 males with IDD, aged 18 years and older, and living in various residential settings across 50 states. Participants ranged in age from 18 to 86 years ($M = 38.84$, $SD = 14.27$). Eighty-nine percent of the participants were Caucasian, 6% African American, 1.5% Hispanic and 3% other racial identities. Twenty-five percent of participants had Down syndrome, 13% cerebral palsy, and 12% autism or pervasive developmental disorder. Over half (56%) of the participants were living with a family member or relative, 29% were

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living on their own, and 14% were living in a foster home or group home. This longitudinal study used the Longitudinal Health and Intellectual and Developmental Disability Survey (LHIDDS) to collect data and examined the relationships among modifiable health behaviors, risk factors, chronic health conditions, psychosocial well-being, and social participation of adults with IDD. Hsieh et al. (2012) provides a detailed description of this survey. An expert panel reviewed the questions in the survey for content, clarity, and significance to the target population and provided feedback on each item after the development of survey using a comprehensive review of existing health survey instruments (e.g., National Health and Nutrition Examination Survey, National Health Interview Survey, Behavioral Risk Factor Surveillance Survey, University of Michigan Health Risk Appraisal Questionnaire). Then, the survey was pilot tested for usability and item clarity with a sample of 10 informants. Test–retest reliability was done with 15 primary caregivers and 15 direct support staff, with test–retest intervals ranging from 2 weeks to 6 weeks. Approximately 52% of the retests were conducted within 2 weeks, 21% within 2–3 weeks, and 27% within 3–6 weeks. For the categorical questions, test–retest reliability (k-statistic) ranged from 0.68 to 0.95 and for the interval questions, the test–retest reliability (intraclass correlation coefficient) ranged from 0.75 to 0.94.

Procedure

The study recruited family members or primary caregivers of adults with IDD by asking families at Special Olympics events, posting or distributing recruitment information through various avenues (e.g. Facebook, newsletter advertisements, and conferences), collaborating with managed care organizations, and communicating about the study with various service agencies. We used a mixed-method (mail and online surveys) data collection procedure **to reach more**

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participants. Informants were asked to complete a paper or online survey, depending on their preference.

Measures

The outcome measure in this analysis was reported high cholesterol status. The independent variables included three factors: (1) demographic, (2) chronic health conditions, and (3) physical inactivity.

Reported high cholesterol status. We asked the informants “Does he/she have high cholesterol based on a diagnosis from a doctor?” The variable was defined as 1 (yes) for having a high cholesterol diagnosis and 0 (no) for not having a high cholesterol diagnosis.

Demographic factors. Demographic information included age, sex, and residence type (own home, family home, or foster/group home).

Chronic health conditions. Chronic health conditions included diabetes and obesity. *Diabetes.* We asked the informants “Does he/she have diabetes (type 1 or type 2) based on a diagnosis from a doctor?” The variable was defined as 1 (yes) for having a diabetes condition and 0 (no) for not having a diabetes condition. *Obesity status.* Obesity was determined by Body Mass Index (BMI), which was calculated using the following formula: $BMI = \text{weight (kg)} / [\text{height (m)}]^2$. Weight and height were informant-reported. Obesity was defined as a BMI equal to or greater than 30 kg/m².

Physical inactivity. Physical inactivity was defined as “never/rarely did moderate and vigorous physical activities”. Informants were asked two separate questions: (1) ‘How many days a week does the person with IDD do moderate physical activities for at least 30 minutes on average?’ and (2) ‘How many days a week does he/she do vigorous activities for at least 20 minutes?’. The responses included “Never/rarely”, “1 or 2 times a week”, “3 times a week”, and

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“4 or more times a week”. Physical inactivity was coded as 1 (when participants responded “Never/rarely” to both of the questions) or 0 (when participants reported having engaged in any frequency of moderate or vigorous physical activities).

Data Analysis

Data was summarized using descriptive statistics. Prevalence of reported high cholesterol was calculated by age, sex, living arrangement, and obesity status. Trend analysis using Cochran-Armitage trend test was conducted to look for any significant effects of prevalence of the outcome and the independent variables across time. **Trend tests included the participants who completed data for the outcome variable (reported high cholesterol) and the modifiable risk factors (obesity, diabetes, and physical inactivity) (See Table 2) at all the four time points.** A generalized estimating equations (GEE) model was constructed in SAS version 9.4 to examine whether chronic conditions (obesity and diabetes) and physical inactivity were associated with reported high cholesterol after adjusting for the demographic factors. Mediating effects of the independent variables on reported high cholesterol were assessed. **Baron and Kenny’s (1986) steps were used to determine the mediation effect. Three regression equations were tested. The first equation tested if the initial variable significantly predicts the outcome variable. The second equation tested if the initial variable significantly predicts the mediator. In the third equation, both the initial variable and the mediator were entered simultaneously and were used to predict the criterion variable. Four criteria must be met to determine the mediation effect.** Mediation is established if the first and the second equations are shown to be significant. In addition, two criteria must be met in the third equation: the mediator must significantly predict the criterion variable and the direct relationship between the initial variable and the criterion variable must be

reduced to zero in the second equation in order to establish full mediation. If the initial variable is reduced in absolute size but is different from zero when the mediator is controlled, partial mediation can then be concluded. Finally, we performed Sobel's (1982) test of significance to determine the extent to which a mediator contributed to the total effect on the criterion variable. A significance level at a p value of 0.05 was used for all analyses.

Results

Prevalence Rates of High Cholesterol by Participant Characteristics at Baseline

Table 1 presents the prevalence rates of reported high cholesterol by participant characteristics at baseline. The mean age of participants who had reported high cholesterol was 46.4 years (SD = 15.01, range = 19-85 years). The prevalence rate of reported high cholesterol significantly increased with age: 9.4% for 18-44 years, 21.9% for 45-64 years and 38.6% for 65 years and above (38.6%), $X^2(2, N = 1,618) = 77.21, p < 0.001$. The prevalence rate of reported high cholesterol was higher among those living in group/foster homes (23.6%), compared to those living on their own (17.6%) and those living with family (10.1%), $X^2(2, N = 1,547) = 32.39, p < 0.001$. The reported high cholesterol rate was higher among those who were obese (19.4%) rather than non-obese (10.7%), $X^2(1, N = 1,523) = 22.51, p < 0.001$; among those who had diabetes (40.0%) compared to those who did not have diabetes (12.1%), $X^2(1, N = 1,617) = 69.15, p < 0.001$; and among those who were physically inactive (17.9%) rather than those who were physically active (12.6%), $X^2(1, N = 1,618) = 7.53, p < 0.01$.

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Insert Table 1

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Prevalence of Outcome and Predictor Variables over Time

Table 2 shows the prevalence of the outcome and the predictor variables of only those participants who responded to these variables across all time points. The prevalence of reported high cholesterol increased over time (12.2% in Year 1, 14.7% in Year 2, 15.5% in Year 3, and 16.0% in Year 5). The Cochran-Armitage trend test showed that the trend was significant ($p=0.03$). The prevalence of obesity was stable over time (24.1% in Year 1, 24.4% in Year 2, 26.5% in Year 3, and 25.0% in Year 5), while diabetes prevalence increased over time albeit non-significantly ($p=0.20$) (5.7% in Year 1, 6.2% in Year 2, 6.2% in Year 3, and 7.3% in Year 5). The prevalence of physical inactivity increased over time but not at a level of statistical significance ($p=0.18$) (28.3% in Year 1, 29.2% in Year 2, 28.9% in Year 3, and 32.0% in Year 5).

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Insert Table 2
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Results of Generalized Estimating Equations (GEE)

Table 3 summarizes the GEE results of the four working correlation specifications. The lowest quasi-likelihood under the Independence Model Criterion (QIC) led to choose the M-dependent correlation model (3732.02) for analysis. Although the M-dependent correlation model gave the lowest QIC results, the estimated coefficients of the four models were also very close. In general, no significant sex effect was found. After multivariate adjustment, older age (45-64 years: OR=1.10, $p < 0.0001$; 65 years and above: OR=1.30, $p < 0.0001$), obesity

(OR=1.07, $p < 0.0001$) and diabetes (OR=1.21, $p < 0.0001$) were significantly associated with reported high cholesterol status. Physical inactivity turned out insignificant.

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Insert Table 3

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Mediator Effect of Diabetes on Association of Obesity and Reported High Cholesterol

Existing literature suggests that obesity is a risk factor for both reported high cholesterol and diabetes (New York State Department of Health, 2016). Therefore, diabetes could serve as a mediating effect on the association between obesity and reported high cholesterol. Mediation effect was tested across the four time points. To test for mediation, three regression equations were conducted for each purpose at each time point. At baseline, the outcome (reported high cholesterol) was regressed on the predictor variable (obesity). This relationship was significant ($b = 0.12$, $p < 0.0001$); therefore, second and third equations proceeded. In the second equation, the mediator (diabetes) was regressed on the predictor variable (obesity). The result indicated that there was a significant relationship between the mediator and predictor variable ($b = 0.14$, $p < 0.0001$). The third equation involved regressing the outcome (reported high cholesterol) variable simultaneously on the predictor (obesity) and mediator variable (diabetes). Since the predictor variable was reduced in absolute size but not zero when the mediator was controlled ($\beta = 0.09$, $p < 0.0001$), partial mediation was concluded. The Sobel test for significance of mediator was 4.57. Since Sobel $z > 1.96$, there was a significant mediating effect. The results also showed that 24.1% of total effects were explained by the mediator; therefore, there was a partial mediator effect of diabetes in the relationship between obesity and reported high cholesterol. The partial

mediation effect was found across all four time points (Table 4). Figure 1 shows the mediation effect graphically.

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Insert Table 4 and Figure 1

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Discussion

The results showed (after adjusting for age, sex, and residence type) that obesity and diabetes were predictive of reported high cholesterol in adults with IDD. These findings underline the need for the relationship between obesity and diabetes, and their association with reported high cholesterol, to be addressed within the IDD community.

Previous studies on the prevalence of diabetes among adults with IDD compared to the general population have provided varied results (MacRae et al., 2015; Reichard & Stolzle, 2011). The prevalence of reported diabetes in our study was 7.11% while prevalence rates ranged from 0.45-25% in other studies (MacRae et al., 2015). A few studies reported significantly higher rates of diabetes in people with IDD than the general population (de Winter, Hermans, Evenhuis, & Echteld, 2015; Reichard & Stolzle, 2011). However it is of note that de Winter et al. (2015) measured serum blood glucose for the diagnosis of diabetes, and Reichard and Stolzle (2011) based their study on self-reported surveys. This variation in the methods of data collection and determination of diabetes status likely contributes to the varying prevalence rates of diabetes, thereby causing difficulty in comparisons of results. Regardless of varying prevalence rates, diabetes (along with obesity), remains a modifiable risk factor that deserves the focus of interventions among this population.

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Interestingly, there was a partial mediator effect of diabetes in the relationship between obesity and high cholesterol in the present study. The partial mediation effect was found across all time points. The mediation effect of diabetes could be explained by the fact that obesity is a risk factor for both reported high cholesterol and diabetes (New York State Department of Health, 2016); or, the effect could be explained by the multiple, interrelated factors associated with metabolic syndrome (Williams, 2002). Further studies are needed to explain the complex mechanisms, including pre-existing IDD-related diagnoses causing these effects.

While high cholesterol prevalence in the U.S., based on National Health and Nutrition Examination Survey (NHANES), is high among all populations (National Center for Health Statistics, 2016), the prevalence of high cholesterol among adults with IDD is substantially higher. The prevalence rate of reported high cholesterol at baseline in adults aged 20 years and above in our study was 14.4%. **Our study did not compare the prevalence rates of high cholesterol in adults with IDD with adults without disability. However, some studies that compared high cholesterol prevalence rates between adults with IDD and adults without disabilities (Henderson et al., 2008; Rimmer, Braddock, & Fujiura, 1994) reported that adults with IDD had higher cholesterol rates compared to adults without disabilities. Our results thus support the reports of previous studies (de Winter et al., 2009; National University of Singapore, 2013; Sohler et al., 2009) which also show that the adults with IDD are more prone to having high cholesterol compared with the general population.** While this population tends to exercise less, be more obese, and have poorer dietary habits (owing to reasons such as lack of day services, skilled staff, dietary advice as well as lifestyle changes and genetic predisposition) (Biswas, Shaherbano, & Hiremath, 2016), they also seem to get fewer health screenings (National University of Singapore, 2013) thereby a likelihood of having higher

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cholesterol levels. Sohler and colleagues (2009) present evidence of high cholesterol becoming more prevalent in the IDD population and affecting people with IDD at younger ages than the general population as shown in our study. Similar to the prevalence rates of diabetes in the general population versus the IDD population, the variations occurring could be due to the differences in data collection methods. For instance, our study used informant-reported surveys. National Center for Health Statistics (2016) used the criteria for hypercholesterolemia as either measured serum total cholesterol greater than or equal to 240 mg/dL) or reporting taking cholesterol-lowering medications. **The study by Rimmer and colleagues (1994), and the study at National University of Singapore Study (2013) used fasting blood lipid testing results, while Henderson and colleagues (2008), and Sohler and colleagues (2009) used medical chart reviews to assess high cholesterol in their participants.**

Hence, there is an urgent need for improved intervention strategies to reduce high cholesterol levels in adults with IDD with better prevention approaches, cholesterol screenings, and treatment & management of high cholesterol given the disparities in health and life opportunities in this population. The general physicians and other health professionals need to take responsibility in preventing, diagnosing and treating high cholesterol levels. High cholesterol can be managed if efforts are taken to identify high cholesterol levels through periodic screening and improved clinical treatment measures (Ford, Pearson, Zhao, & Mokdad, 2010). The US Preventive Services Task Force (USPSTF) advocates a targeted cholesterol screening approach for young adults (men aged 20 to 35 years and women aged 20 to 45 years). The USPSTF recommends screening young adults with CHD, CHD equivalents (other forms of atherosclerotic vascular disease, diabetes, or CHD risk of 20% or greater within 10 years), or one or more CHD risk factors (high blood pressure, smoking, family history, and obesity) (USPSTF,

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2008). However, the adults who do not have CHD or CHD equivalent and may have high cholesterol would theoretically miss out on getting screened with this approach (Kuklina, Yoon, & Keenan, 2010). Additionally, there might be under-recognition of **cardiovascular disease (CVD)** risk factors such as high cholesterol levels because of under-utilization of health screening services in adults with IDD (Janicki et al., 2002). Therefore, the gap in screening among adults with IDD needs to be addressed. Future studies are needed to identify how cholesterol screening among adults with IDD can be included and improved upon in community settings.

Strengths of the present study are the large sample size and the wide range of demographic, health-and-function-related, and socio-environmental factors included in the data collection as well as the use of GEE for the longitudinal analysis. The study's main limitation is the use of informant reports to measure physical inactivity and sedentary time, which is subject to recall bias and socially desirable answers. The fact that the definition of reported high cholesterol in the present study is based on the question asked to informants (whether the adult with IDD has high cholesterol based on a diagnosis from a doctor) rather than on objective measurements of biomarkers or medical records could also be a limitation of the study.

Additionally, informant-reported high cholesterol could be under-reported, especially when the persons with IDD were not taking medication for it. We need to be cautious when interpreting these results as the measures were based on proxy reporting, which is not the ideal method to collect data on chronic health conditions. The recruitment and consent procedures could also have led to biases within this study. Furthermore, the sample was not representative of the US population in terms of ethnicity or race, which limits the generalizability to other subgroups with IDD.

Conclusion

Prevalence of high cholesterol increases with age among adults with IDD. Adults with IDD who have diabetes and obesity may have a higher risk of developing high cholesterol which may cause heart disease. Obesity and diabetes are preventable through regular physical activity and healthy diets. However, further research studies are needed to advance our knowledge on the complex mechanisms behind the relationships between diabetes, obesity, high cholesterol and heart disease and pre-existing conditions of adults with IDD. Additionally, efforts to prevent and reduce high cholesterol in adults with IDD need to be taken by key stakeholders such as physicians, community service providers, caregivers and other health professionals. There is also a great need to improve and impart health education and health promotion strategies for adults with IDD to community personnel and caregivers.

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Table 1. Prevalence of Reported High Cholesterol by Participant characteristics at Baseline

	Total (N=1,618)	High cholesterol (n=227)		χ^2 or t
		Mean	SD	
Age	46.42	46.42	15.01	-9.59***
	N	N	%	
Age groups				77.21***
18-44 years	1,109	104	9.38	
45-64 years	439	96	21.87	
≥ 65 years	70	27	38.57	
Sex				1.00
Male	892	123	13.79	
Female	726	104	14.33	
Diagnostic group				6.79
ID only and others	745	114	15.30	
Autism	181	17	9.39	
Cerebral Palsy	189	21	11.11	
Down syndrome	372	43	11.56	
Level of ID				3.10
Borderline	201	29	14.43	
Mild or moderate	848	115	13.56	
Severe or profound	132	11	8.33	
Residence				32.39***
Own home	455	80	17.58	
Family home	872	88	10.09	
Foster/group home	220	52	23.64	
Obesity				22.51***
Yes	578	112	19.38	
No	945	101	10.69	
Diabetes				69.15***
Yes	115	46	40.00	
No	1,502	181	12.05	
Physical inactivity				7.53**
Yes	448	80	17.86	
No	1,170	147	12.56	

Note. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Table 2. Prevalence of predictor and outcome variables over time

Variable	N	Year 1	Year 2	Year 3	Year 5	Cochrane- Armitage trend test p value
		%	%	%	%	
Outcome						
Reported High cholesterol	784	12.2	14.7	15.5	16.0	0.0310
Modifiable risk factors						
Obesity	703	24.1	24.4	26.5	25.0	0.3513
Diabetes	784	5.7	6.2	6.2	7.3	0.2037
Physical inactivity	644	28.3	29.2	28.9	32.0	0.1766

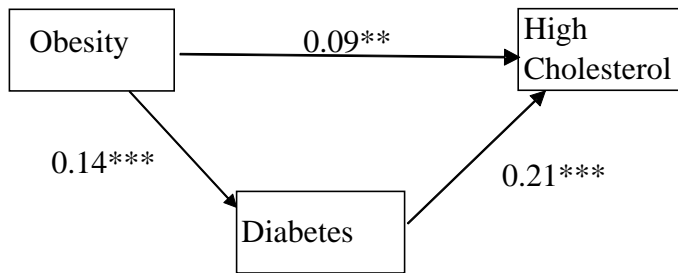
Table 3. Factors associated with Reported High Cholesterol using GEE model

Variable	M Dependent			
	OR	SE	95% CI	p value
Age group				
18-44 years (ref)				
45-64 years	1.10	0.02	1.06-1.14	<0.0001
≥65 years	1.30	0.04	1.19-1.41	<0.0001
Sex (Male)	1.00	0.02	0.97-1.03	0.799
Residence				
Own home (ref)				
Family home	0.97	0.02	0.94-1.01	0.120
Foster/group home	1.02	0.02	0.99-1.06	0.203
Obesity	1.07	0.01	1.04-1.10	<0.0001
Diabetes	1.21	0.04	1.13-1.31	<0.0001
Physical inactivity	1.00	0.01	0.98-1.03	0.918
time	1.00	0.01	0.99-1.01	0.404
QIC			3732.02	

Table 4. Mediator effect of diabetes on association of obesity and reported high cholesterol at baseline

	Unstandardized		Standardized	
	B	SE B	b	P
Step1 - Obesity->High cholesterol				
Obesity	0.08689	0.01819	0.12157	<0.0001
Step2 - Obesity-> Diabetes				
Obesity	0.07493	0.0136	0.13989	<0.0001
Step3- Obesity Diabetes->High cholesterol				
Obesity	0.06599	0.01797	0.09233	0.0002
Diabetes	0.27891	0.03355	0.20903	<0.0001
Test for significance of mediator:				
	4.56961			
% total effects explained by mediator:				
	24.1%			
Direct effect				
	0.09233			
Indirect effect				
	0.02924			
Total effect				
	0.12157			

Figure 1. Diabetes as a **Partial Mediator** of Obesity and Reported High Cholesterol



p<0.001*p<0.0001