

Differences in HDL Subfraction  
Distribution in Normolipidemic  
Versus Dyslipidemic Individuals.

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# Introduction

HDL encompasses a heterogeneous class of lipoprotein subclasses that differ in composition and physiological function and may vary in their anti-atherogenic potential and utility as markers for CHD risk. Lipoprotein heterogeneity has been demonstrated by various analytical methods such as density gradient ultracentrifugation, nuclear magnetic resonance (NMR), non-denaturing gradient gel electrophoresis (GGE), polyionic precipitation methods, and linear polyacrylamide gel electrophoresis.

# Introduction cont.

Traditionally, HDL has been separated into two major subclasses (HDL2 and HDL3). Depending on the separation method used, three or more subfractions have been reported. Using linear polyacrylamide gel electrophoresis, we were able to derive subfractions that have been grouped into three main subclasses; Large HDL, HDL(L), Intermediate HDL, HDL(I) and Small HDL, HDL(S).

# Introduction cont.

It appears that most changes in HDL cholesterol resulting from genetic and environmental changes or treatment with lipid lowering drugs are mostly attributed to HDL2. The question is whether measuring HDL subfractions is of greater predictive value for assessing CHD risk than total HDL cholesterol. Many studies identify HDL-2 as the most antiatherogenic and is most strongly associated with CHD.

# Introduction cont.

Some early studies have questioned the benefit of these subfractions in potentially identifying risks for CHD or ischemic heart disease (IHD). The accuracy of the method used for the separation of the HDL subfractions as well as the manner in which the studies were conducted has been questioned. These reports agree that further studies need to be undertaken due to the inconsistency of the measurements from the different methods which do not necessarily agree on the composition and activity of the HDL subfraction measured and the sample size of the study. Given these facts, it should be concluded that measurements of HDL subfractions are of significance.

# Test Principle

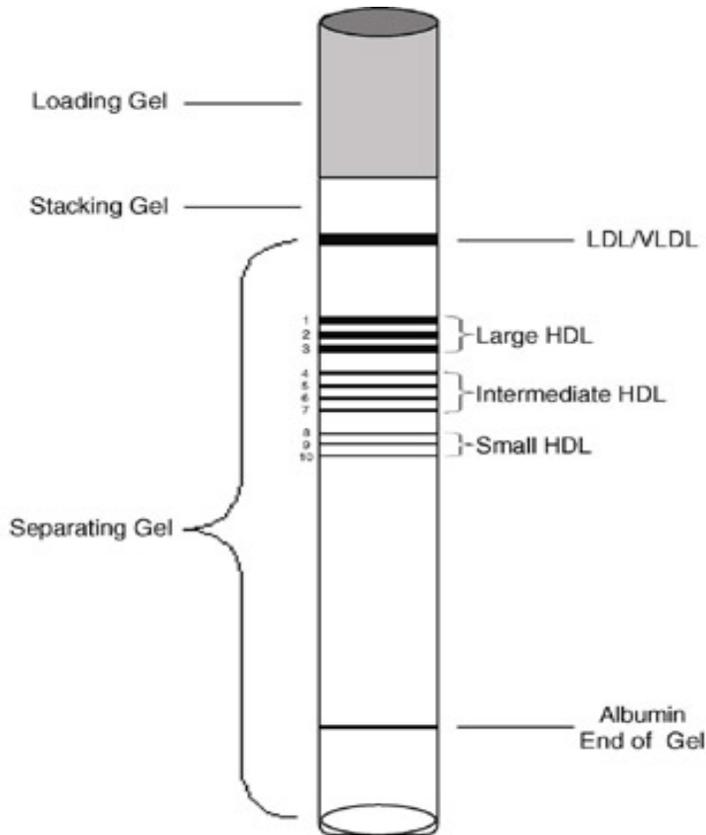


Figure 1. Linear polyacrylamide electrophoresis Gel Tube Schematic

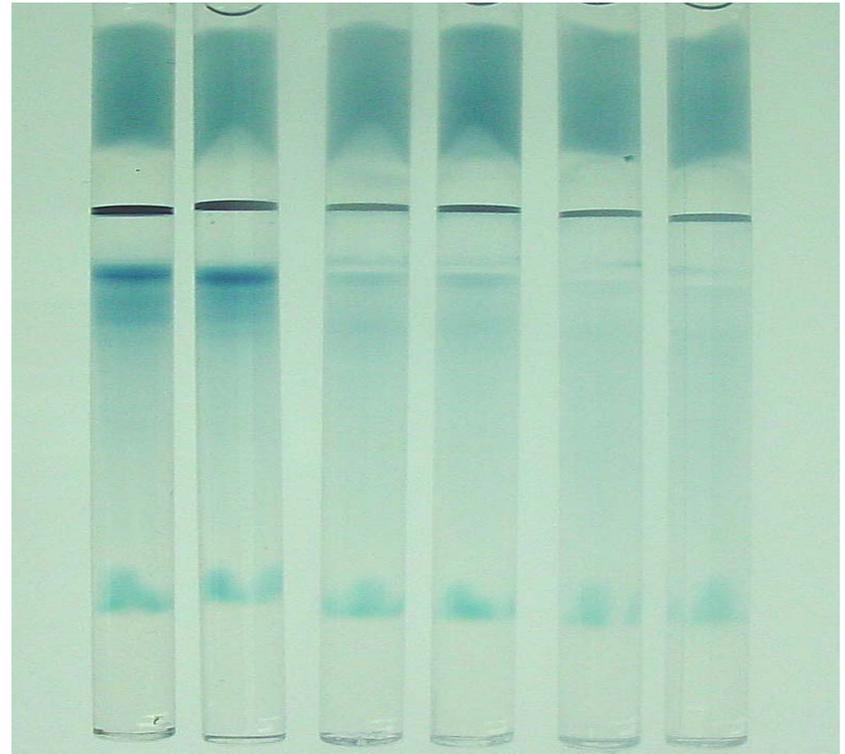
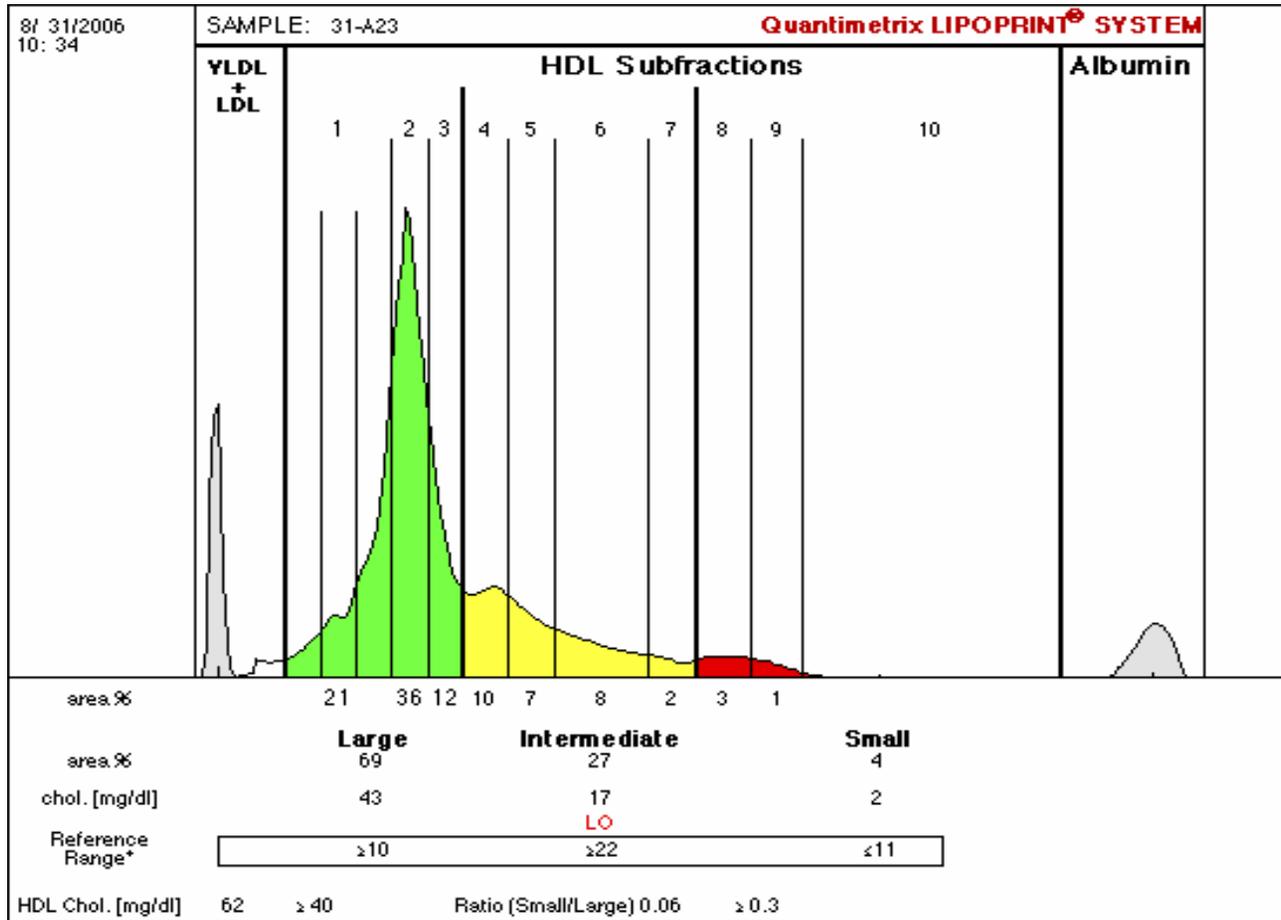


Figure 2. Linear Polyacrylamide Electrophoresis Gel Tubes after electrophoresis of a Normal, Intermediate & Abnormal Human Serum Lipid Samples.

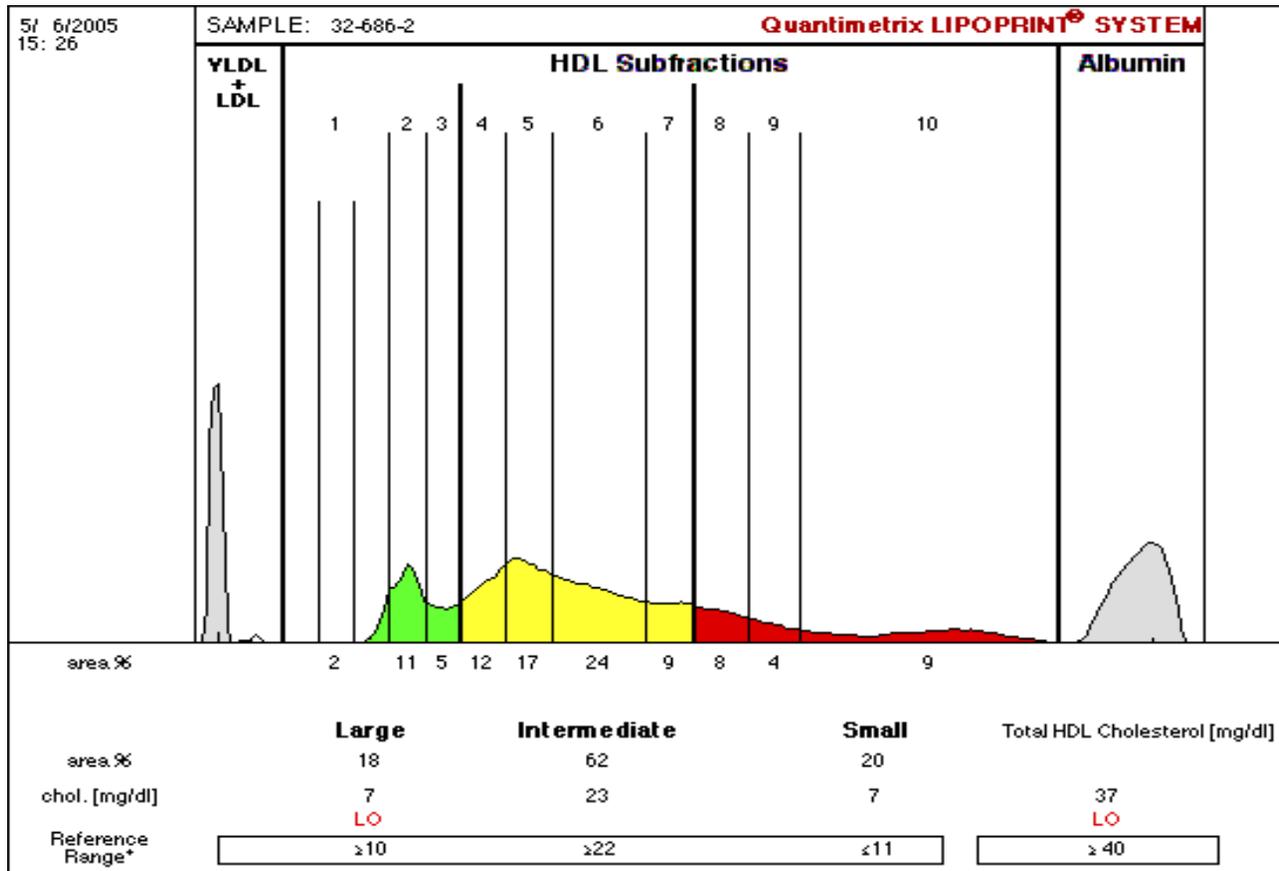
# Profiles



\*Reference ranges derived from 123 serum samples that met the NCEP ATPIII guidelines for desirable lipid status

## Normal Profile

# Profiles cont.

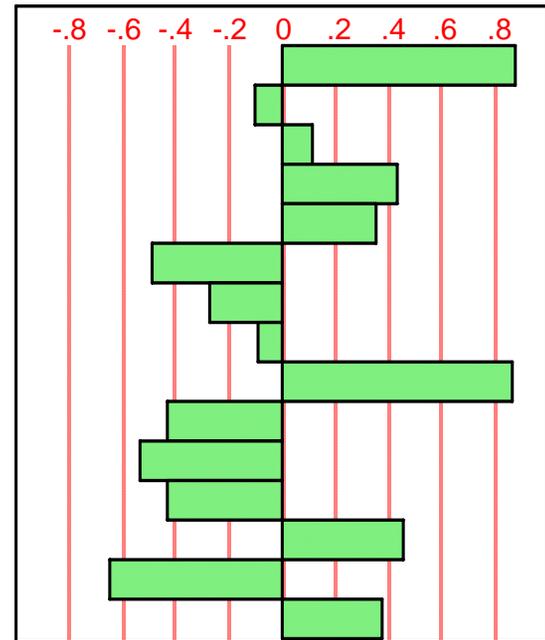


Non-normal Profile

# Results

## Nonparametric Measures of Association

Variable	by Variable	Spearman Rho	Prob> Rho
m HDL-C	HDL-L	0.8787	<.0001
m TC	HDL-L	-0.1012	0.0711
m TC	HDL-C	0.1214	0.0301
m Particle Size	HDL-L	0.4429	<.0001
m Particle Size	HDL-C	0.3598	<.0001
m Particle Size	TC	-0.4874	<.0001
m LDL-C	HDL-L	-0.2712	<.0001
m LDL-C	HDL-C	-0.0850	0.1300
m LDL-C	TC	0.8708	<.0001
m LDL-C	Particle Size	-0.4247	<.0001
m Trigs	HDL-L	-0.5327	<.0001
m Trigs	HDL-C	-0.4210	<.0001
m Trigs	TC	0.4606	<.0001
m Trigs	Particle Size	-0.6460	<.0001
m Trigs	LDL-C	0.3762	<.0001

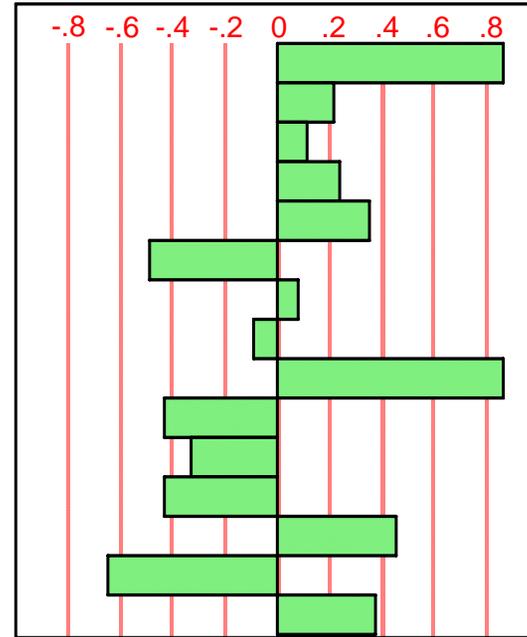


Non-parametric Measures of Association for HDL-L  
Subfraction

# Results cont.

## Nonparametric Measures of Association

Variable	by Variable	Spearman Rho	Prob> Rho
m HDL-C	HDL-I	0.8652	<.0001
m TC	HDL-I	0.2196	<.0001
m TC	HDL-C	0.1214	0.0301
m Particle Size	HDL-I	0.2467	<.0001
m Particle Size	HDL-C	0.3598	<.0001
m Particle Size	TC	-0.4874	<.0001
m LDL-C	HDL-I	0.0844	0.1326
m LDL-C	HDL-C	-0.0850	0.1300
m LDL-C	TC	0.8708	<.0001
m LDL-C	Particle Size	-0.4247	<.0001
m Trigs	HDL-I	-0.3185	<.0001
m Trigs	HDL-C	-0.4210	<.0001
m Trigs	TC	0.4606	<.0001
m Trigs	Particle Size	-0.6460	<.0001
m Trigs	LDL-C	0.3762	<.0001

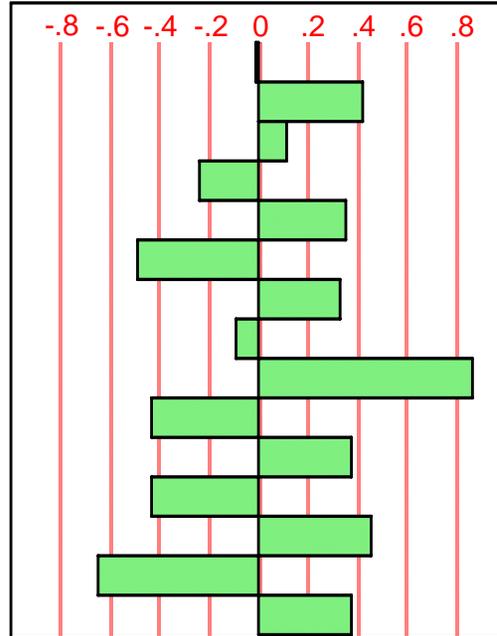


Non-parametric Measures of Association for HDL-I  
Subfraction

# Results cont.

## Nonparametric Measures of Association

	Variable	by Variable	Spearman Rho	Prob> Rho	
m	HDL-C	HDL-S	-0.0015	0.9788	
m	TC	HDL-S	0.4206	<.0001	
	TC	HDL-C	0.1214	0.0301	
m	Particle Size	HDL-S	-0.2308	<.0001	
	Particle Size	HDL-C	0.3598	<.0001	
	Particle Size	TC	-0.4874	<.0001	
m	LDL-C	HDL-S	0.3296	<.0001	
	LDL-C	HDL-C	-0.0850	0.1300	
	LDL-C	TC	0.8708	<.0001	
	LDL-C	Particle Size	-0.4247	<.0001	
m	Trigs	HDL-S	0.3800	<.0001	
	Trigs	HDL-C	-0.4210	<.0001	
	Trigs	TC	0.4606	<.0001	
	Trigs	Particle Size	-0.6460	<.0001	
	Trigs	LDL-C	0.3762	<.0001	



Non-parametric Measures of Association for HDL-S  
Subfraction

# Results cont.

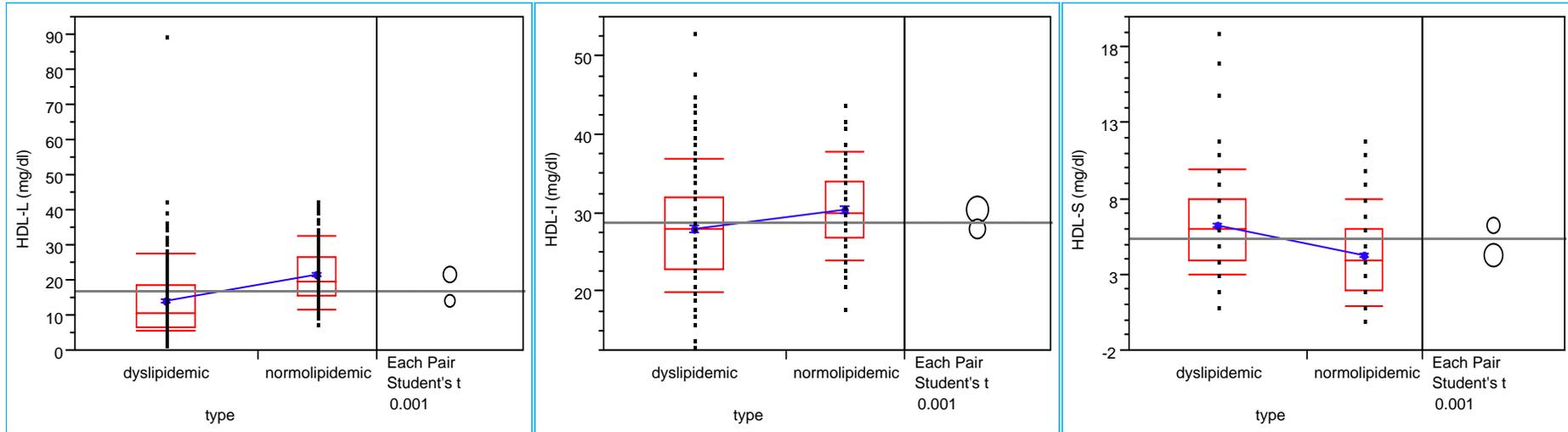
	HDL Large [mg/dl]	HDL Intermediate [mg/dl]	HDL Small [mg/dl]	HDL total [mg/dl]	CHOL total [mg/dl]
range	8 - 43	18 - 44	0 - 12	40 - 89	110 - 199
mean	21.7	30.4	4.3	56.5	166.2
SD	8.05	5.06	2.56	10.87	19.37
95% range	10.0- 41.9	22.0-41.9	1.0-11.0	41.0-79.9	118.5-197.8
N*	123	123	123	123	123

**Table 1. Normolipidemic population**

	HDL Large [mg/dl]	HDL Intermediate [mg/dl]	HDL Small [mg/dl]	HDL total [mg/dl]	CHOL total [mg/dl]
range	2 - 90	13 - 53	1 - 19	21-122	94 - 322
mean	14.5	28.1	6.2	49.0	213.9
SD	10.3	7.01	3.05	15.54	39.17
95% range	3.8 - 37.0	16.8 - 43.2	1.0 - 12.6	27.0-85.8	124.6-299.4
N*	191	191	191	191	191

**Table 2. Dyslipidemic population**

# Results cont.



**Figure 3. Plot of HDL-L, HDL-I, and HDL-S vs. sample type**

# Conclusions

- The large HDL subfractions, HDL-L showed a significant positive correlation with HDL-C and a slight positive correlation with particle size. A slight inverse relationship was found with triglyceride and no correlations with total cholesterol and LDL-C.
- The intermediate HDL subfractions, HDL-I also exhibited a significant positive correlation with HDL-C. No correlations were found with total cholesterol, triglycerides, particle size and LDL-C.
- The small HDL subfractions, HDL-S exhibited a slight positive correlation with total cholesterol. No correlations were found with HDL-C, particle size, triglycerides, and LDL-C.

# Conclusions cont.

- Comparison of the HDL subclasses, Large HDL (HDL-L), Intermediate HDL (HDL-I) and Small HDL (HDL-S) between the normolipidemic and dyslipidemic samples showed that there is significant difference between the means of the two samples ( $P < 0.001$ ) for the HDL-L and HDL-S but not for the HDL-I ( $P < 0.0015$  ).
- The Large HDL subclass (HDL-L) showed an inverse relationship with CHD risk factors while the Small HDL subclass (HDL-S) exhibited a direct relationship with CHD risk factors.