Time-Dependent Change in High Density Lipoprotein Cholesterol and the Risk of Subsequent Cardiovascular Disease in Apparently Healthy Individuals

Assi Milwidsky, Shaye Kivity*, Eran Kopel*, Diego Medvedofsky*, Robert klempfner*, Anat Berkovitch, Fernando Chernomordik*, Yechezkel Sidi***, Ilan Goldenberg*, Elad Maor***

** Heart institute,*** Internal medicine “C”, Sheba Medical Center, Tel Hashomer, Israel.
* Internal medicine “E” Tel-Aviv medical center, Israel.

Sheba Medical Center
Tel Hashomer

The Leviev Heart Center

Conflict of interest

- None

BACKGROUND

- High-density lipoprotein (HDL) cholesterol is a strong inverse predictor of cardiovascular events.
- However, it is not clear whether changes in HDL levels during follow-up in apparently healthy individuals affect subsequent cardiovascular outcomes.

STUDY AIMS

- Describe changes in HDL among apparently healthy individuals

- Evaluate the prognostic implications of HDL change over time

METHODS

- The study population comprised 10,067 healthy subjects without known cardiovascular disease.
- Subjects underwent a yearly screening program and were followed up for up to 10 years.
- Low HDL was defined as <40 mg/dL for men and <50 mg/dL for women.

DEFINITIONS AND END POINTS

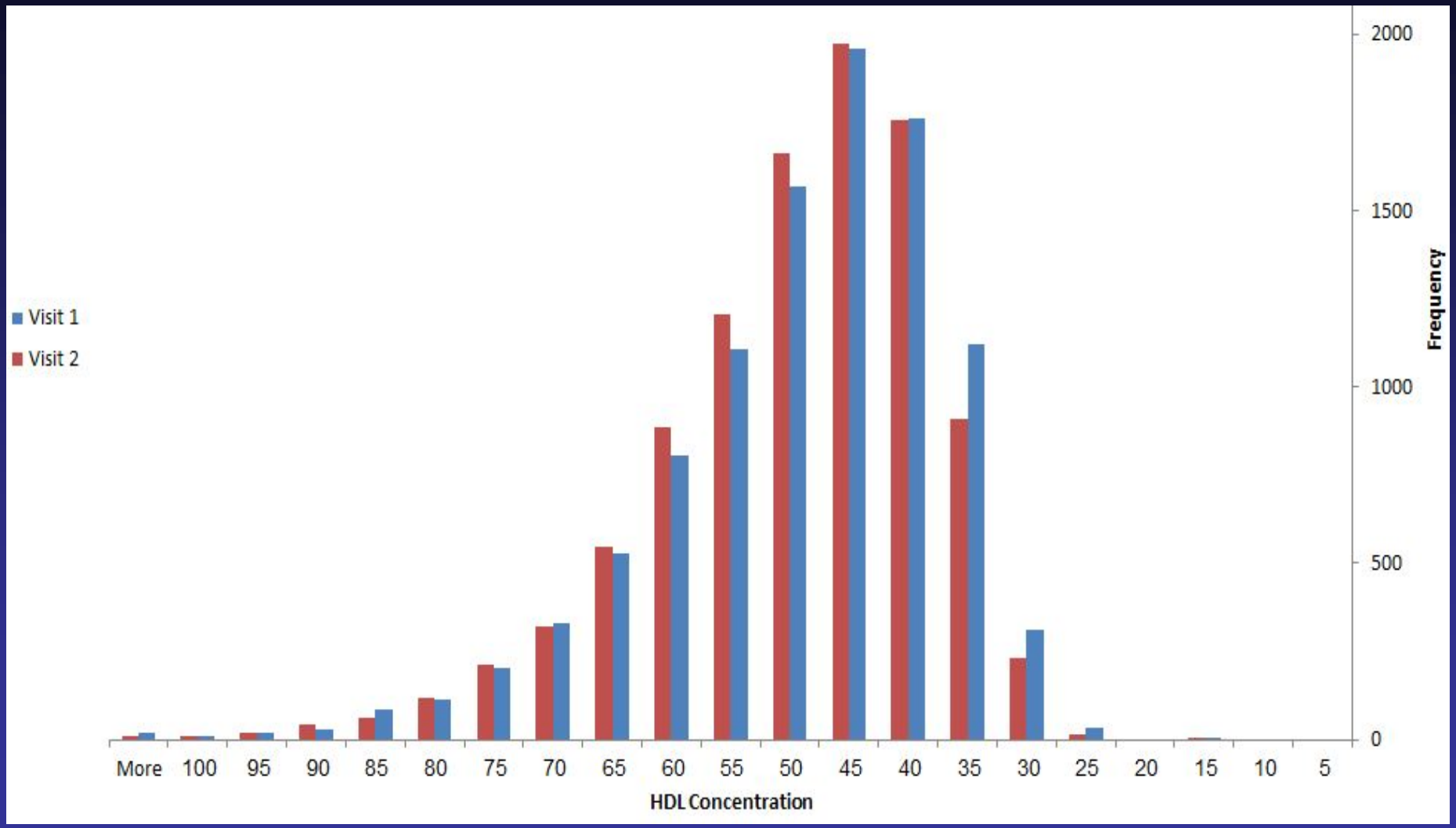
- Participants were grouped into four groups based on change of HDL cholesterol level between the first (baseline) and second (first year follow-up) visits:
  - **High/High (HH)**
  - **High/Low (HL)**
  - **Low/High (LH)**
  - **Low/Low (LL)**
- The primary endpoint - the occurrence of cardiovascular disease, was defined as the composite of – acute coronary syndrome, significant coronary artery disease or PCI

RESULTS

Baseline Characteristics

	N=10,067
Males	75%
Age	50±10 (20-92)
Diabetes mellitus	2%
Hypertension	16%
Number of visits	6.6±2.7 (3-12)
Mean follow up (days)	1,644±1,000
First HDL (mg/dl)	47±12
Second HDL (mg/dl)	48±12
Development of Cardiovascular disease	390 (3.9%)

HDL distribution in the landmark visits



HDL Categories

First Visit	Second Visit (*)	Category	# of Patients
High	High	HH	5,754 (57%)
Low	High	LH	964 (9.6%)
High	Low	HL	797 (7.9%)
Low	Low	LL	2552 (25%)

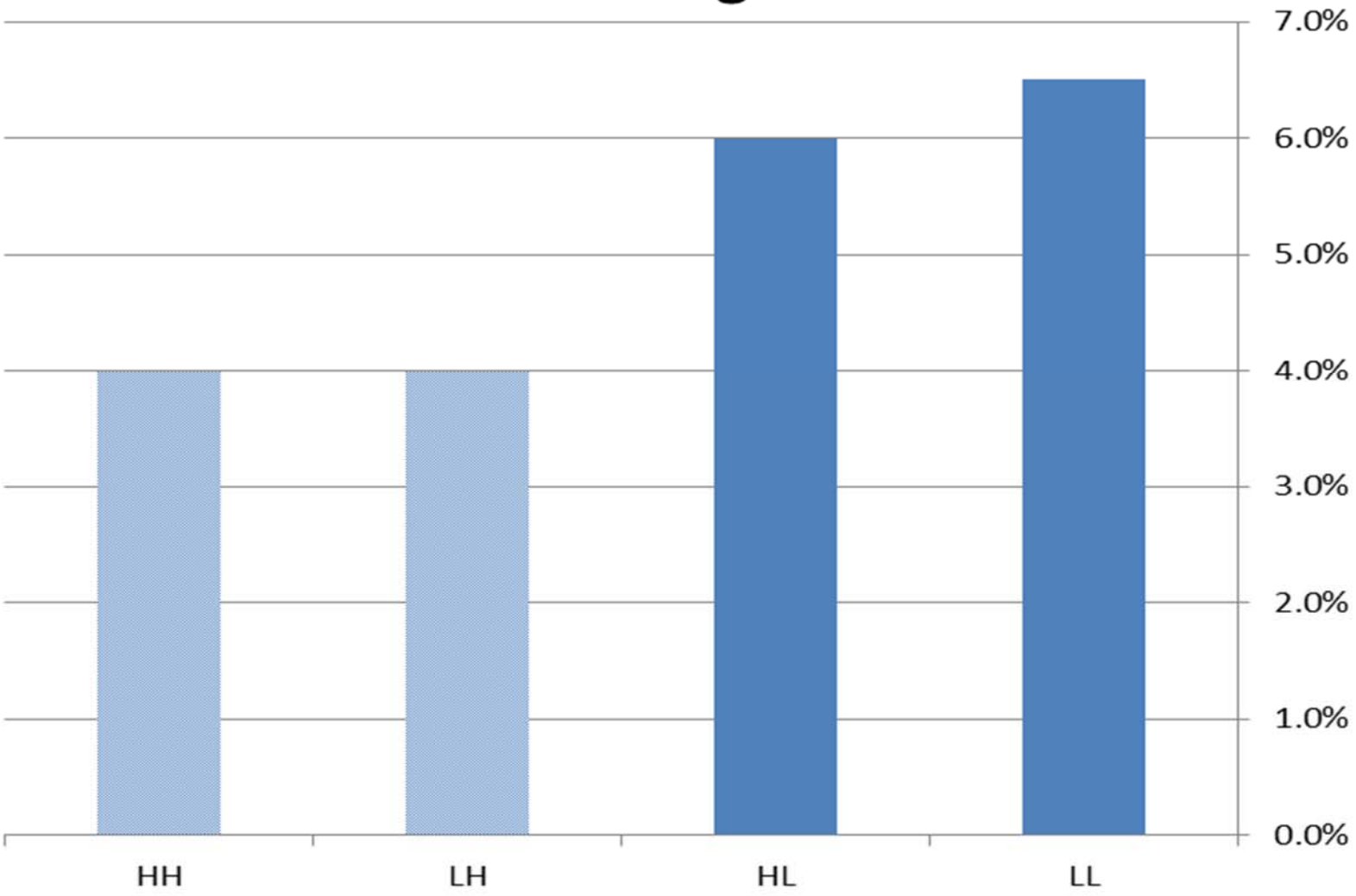
* Paired t-test of HDL between first and second visit: change 0.63 (0.5-0.77), p<0.001

Baseline Characteristics by HDL Categories

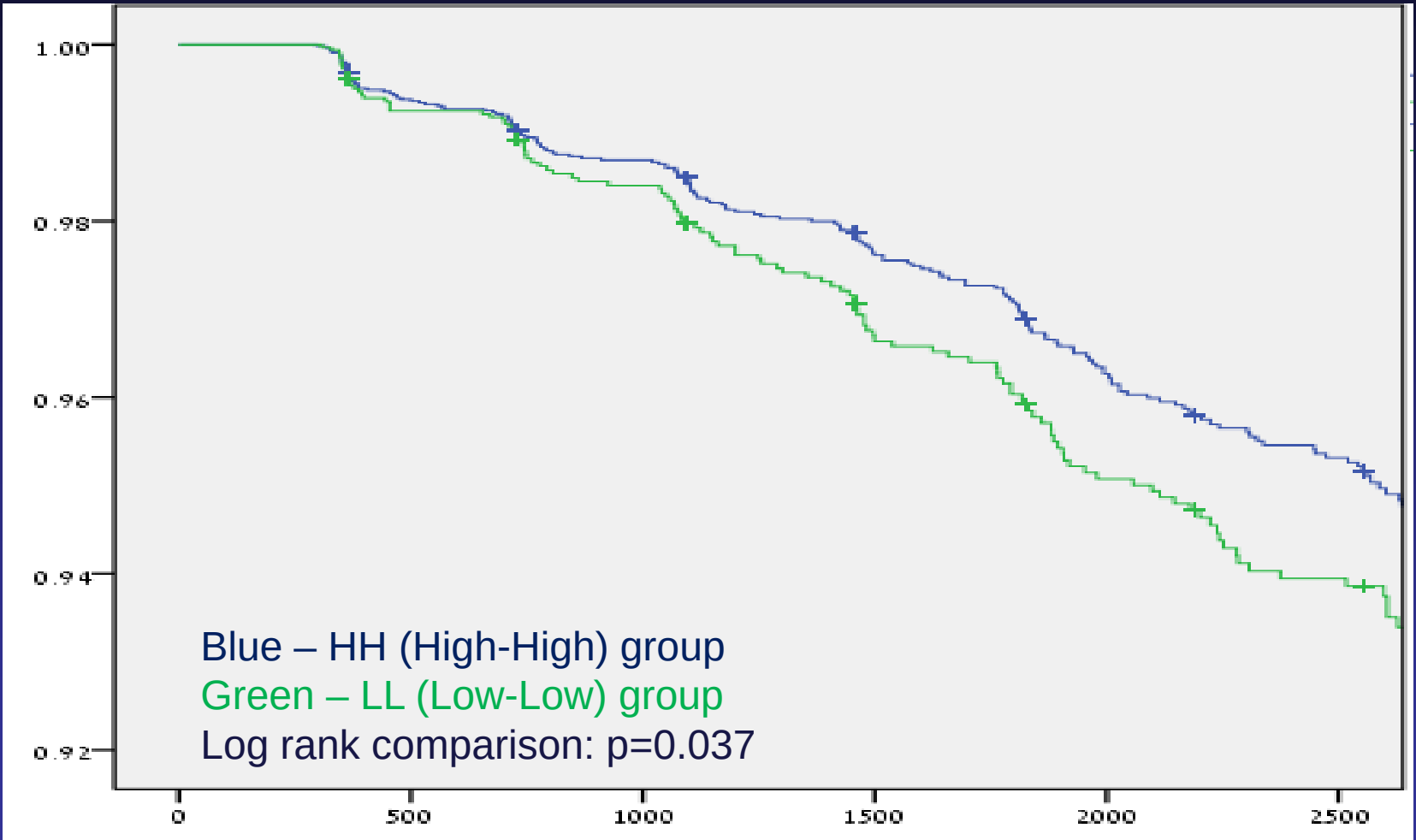
	HH	HL	LH	LL
Age, yrs	51 ± 11	50 ± 10	49 ± 10	50 ± 10
First HDL, mg/d)	53.6 ± 11	46.3 ± 7	38.6 ± 5	35.7 ± 5
BMI, kg/m^2	25.5 ± 3.6	26.6 ± 4	26.6 ± 4	27.3 ± 4
Triglycerides, mg/dl	110 ± 54	140 ± 72	140 ± 69	167 ± 86
LDL, mg/dl	123 ± 28	117 ± 26	129 ± 29	119 ± 27
Blood pressure, mmHg	123/78	124/79	124/79	125/79

* All p <0.05

8 years cardiovascular diseases rates by HDL change



Event Free Survival by HDL Change Groups



Multivariate Analysis: Risk of Events by HDL change Groups*

HDL Category	HR (CI 95%)	P value for trend
LL (Low/Low)	1.00 (reference)	<0.001
HL (High/Low)	0.87 (0.56 - 1.33)	
LH (Low/High)	0.70 (0.46 - 1.05)	
HH (High/High)	0.67 (0.53 - 0.85)	

*Findings are further adjusted for age and gender

Multivariate Analysis: Risk of Events by Baseline and Follow-Up HDL

Covariate	HR (95% CI)	P value
Age	1.07 (1.06 - 1.08)	<0.001
Gender	0.13 (0.08 - 0.22)	<0.001
Low HDL visit 1	1.09 (0.82 - 1.45)	0.557
Low HDL visit 2	**1.36 (1.02 -1.81)**	**0.036**

CONCLUSIONS

- In apparently healthy individuals without known cardiovascular disease:
  - Changes in HDL levels during follow-up are independently associated with subsequent CVD risk.
  - Follow up HDL levels provide incremental prognostic information to baseline levels in this population

CLINICAL IMPLICATIONS

- Risk assessment for primary prevention of CVD should incorporate evaluation of time-dependent changes in HDL levels

The end

Thank you for listening