Training series on "Screening and Evaluation of Comprehensive Intervention for Groups at High Risk of Cardiovascular Disease

# An Overview of Hyperlipidemia

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- **Lipids and Lipoproteins**
- **Clinical significance of the major components of blood lipids**
- **Appropriate lipid levels and dyslipidemia**
- **Summary**

# Lipids and Lipoproteins

- Lipids are a general term for serum cholesterol, triglycerides, and lipoids (e.g., phospholipids), and the main clinically relevant lipids are cholesterol and triglycerides.

- In our body, cholesterol exists mainly as free cholesterol and cholesterol esters; triglycerides are formed when the three hydroxyl groups in the glycerol molecule are esterified by fatty acids.

- Lipids are insoluble in water and must bind to specific proteins called apolipoproteins to form lipoproteins that are soluble in the blood and are transported to tissues for metabolic processes.

Lipoproteins are classified as :

**Chylomicron** (CM)

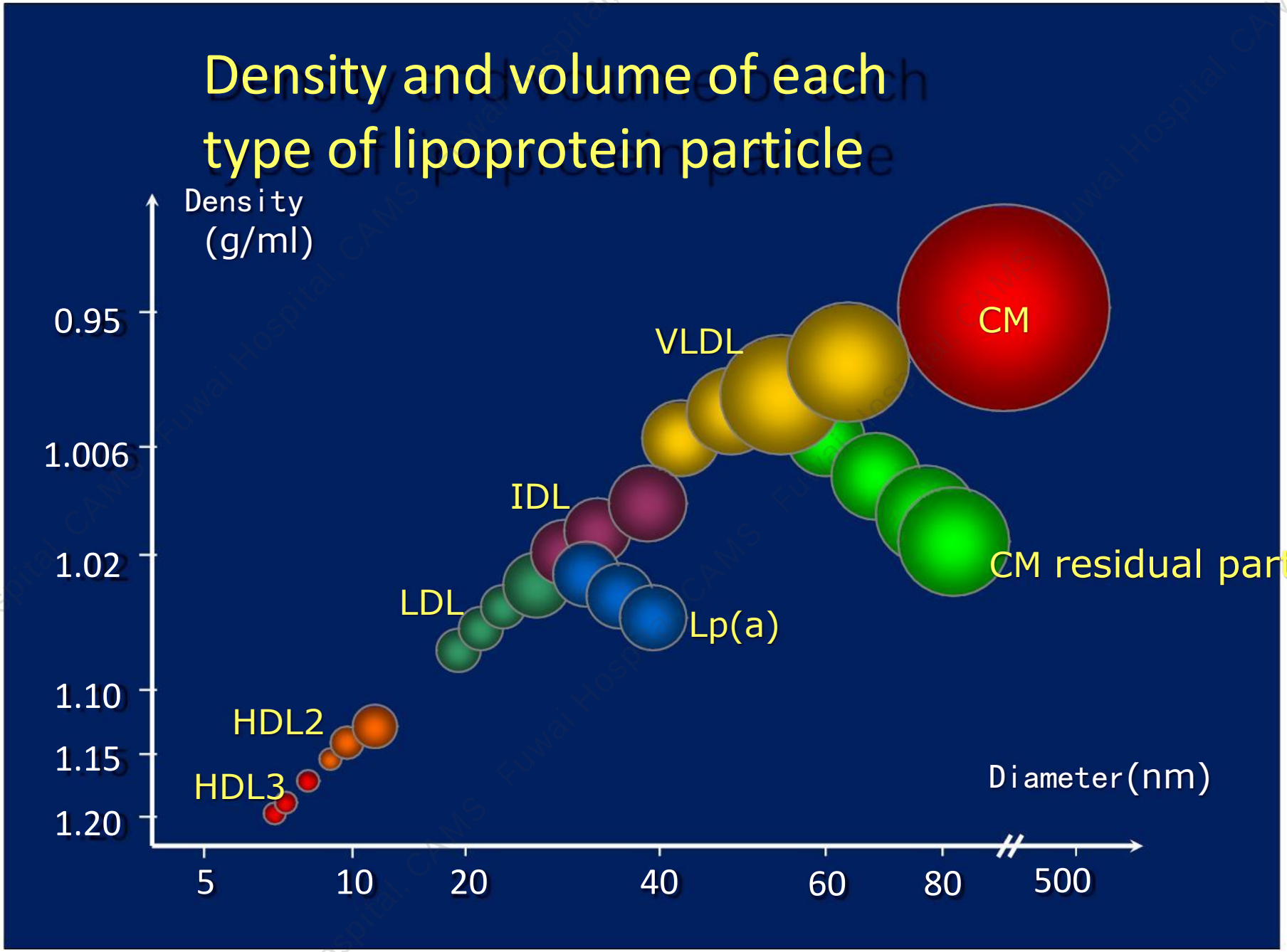
**Very low density lipoprotein** (VLDL)

**Intermediate density lipoprotein** (IDL)

**Low density lipoprotein** (LDL)

**High-density lipoprotein** (HDL)

**Lipoprotein**(a) Lp(a)



# Lipids and Lipoproteins

## Properties and functions of lipoproteins

| Classification | Particle diameter (nm) | Main components | Major Apolipoproteins | Source | Function |
|---|---|---|---|---|---|
| CM | 80~500 | TG | $_{B48}$, A1, A2 | Small intestine synthesis | Transport of food TG and cholesterol from the small intestine to other tissues |
| VLDL | 30~80 | TG | $_{B100}$, E, Cs | Liver synthesis | Transport of endogenous TG to peripheral tissues and release of free fatty acids after lipase hydrolysis |
| IDL | 27~30 | TG, cholesterol | B100, E | TG in VLDL is formed after hydrolysis by lipase | LDL precursor, partially metabolized by the liver |
| LDL | 20~27 | Cholesterol | $_{B100}$ | TG in VLDL and IDL is formed after hydrolysis by lipase | The main carrier of cholesterol, mediated by LDL receptors for uptake and utilization by peripheral tissues, directly related to ASCVD |
| HDL | 8~10 | Phospholipids, cholesterol | A1, A2, Cs | Mainly synthesized by the liver and small intestine | Promotes cholesterol removal from peripheral tissues, transports cholesterol to the liver or other tissues for redistribution, HDL-C negatively correlates with ASCVD |
| Lp(a) | 26 | Cholesterol | , (a) | Complex formation with LDL via disulfide bonds in hepatic apolipoprotein (a) | Possibly related to ASCVD |

Note: CM; celiac particles; VLDL: very low density lipoprotein; IDL; intermediate density lipoprotein; LDL: low density lipoprotein; HDL: high density lipoprotein; Lp(a): lipoprotein(a); TG: triglycerides; ASCVD:100atherosclerotic cardiovascular disease; HDL-C: high density lipoprotein cholesterol

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# Total Cholesterol (TC)

TC is the sum of cholesterol contained in various lipoproteins in the blood serum.

The main factors affecting TC levels are

- **(1) Age and gender:** TC levels often increase with age, but no longer increase or even decrease after 70 years of age, and are lower in young and middle-aged women than in men, and TC levels are higher in women after menopause than in men of the same age.
- **(2) Dietary habits**: Long-term high cholesterol and high saturated fatty acid intake can raise TC.
- **(3) Genetic factors:** Mutations in enzymes or receptor genes related to lipoprotein metabolism are the main cause of significant increases in TC.

The risk assessment and predictive value of TC for atherosclerotic disease is less accurate than that of **LDL-C.**

# Triglycerides (TG)

## Triglycerides (TG)

- TG levels are influenced by both genetic and environmental factors, and are related to race, age, gender, and lifestyle habits (e.g., diet, exercise, etc.). Unlike TC, TG levels are highly variable within and between individuals. TG levels in the same individual are influenced by diet and different time of day, so there may be large differences in TG values when the same individual is measured multiple times. Serum TG levels show a significant positive-skewed distribution in the general population.
- Mild to moderate elevations in TG often reflect an increase in VLDL and its remnants (smaller VLDL particles), which may have direct atherogenic effects due to their smaller particle size. However, most studies suggest that elevated TG is likely to have atherogenic effects by affecting the structure of LDL or HDL.
- People with mild to moderate elevations in serum TG levels are at increased risk for coronary heart disease. When TG is severely elevated, it is often associated with acute pancreatitis.

# Low-density lipoprotein cholesterol (LDL-C)

- Increased LDL-C is a major risk factor for the development of atherosclerosis.
- Although atherosclerotic pathology is characterized by chronic inflammatory response, LDL is likely to be an essential factor in the initiation and maintenance of this chronic inflammation. In general, LDL-C is parallel to TC, but TC level is also affected by HDL-C level. Therefore, LDL-C is a relatively better indicator to evaluate the risk of ASCVD.

LDL-C first enters the endothelial cells

Foam cell formation

Atherosclerotic plaque formation

Narrowing of the inner wall

# High-density lipoprotein cholesterol (HDL-C)

- HDL transport cholesterol from peripheral tissues, such as blood vessel walls, to the liver for catabolism, i.e., cholesterol reversal, which can reduce cholesterol deposition in blood vessel walls and play an anti-atherosclerotic role. Since the cholesterol content of HDL is relatively stable, the level of HDL in the blood is now measured indirectly by measuring the amount of cholesterol it contains.

- HDL-C levels are also significantly influenced by genetic factors. Severe malnutrition is accompanied by a significant decrease in serum TC and a low HDL-C. Obese individuals also tend to have low HDL-C. Smoking can lower HDL-C. Disease states such as diabetes, hepatitis and cirrhosis can be associated with low HDL-C. Patients with HTG (hypertriglyceridemia) tend to have low HDL-C. Exercise and small amounts of alcohol increase HDL-C. A large body of epidemiological data suggests that serum HDL-C levels are negatively associated with the risk of ASCVD.

# The "good" cholesterol and the "bad" cholesterol

Cholesterol is loaded by "empty van" of phospholipids and apolipoproteins to form "transport van" - i.e., lipoproteins, which are transported to various parts of the body. According to the density of the lipids loaded in the "transport van", lipoproteins are classified as:

**The "bad" cholesterol**: low-density lipoprotein cholesterol (LDL-C), the lipid "unloader" that transports cholesterol synthesized in the liver to the blood vessels

**The "good" cholesterol**: HDL-C, the lipid "cleansing vehicle" that picks up excessive cholesterol from the blood vessels and transports it back to the liver


1. Chinese Society of Preventive Medicine, Chronic Disease Prevention and Control Branch, et al. Chinese Journal of Preventive Medicine, 2016,50(11):936-937
2. Gao W, et al. Chinese Journal of Frontiers in Medicine (electronic version), 2011, 3(5):1-3

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# Dyslipidemia

- **Dyslipidemia usually refers to elevated serum cholesterol and/or TG levels, commonly known as hyperlipidemia. In fact, dyslipidemia also refers to a wide range of dyslipidemia, including low HDL-C blood. The classifications are complicated, but the simplest ones are etiologic and clinical classification.**

- **Classification of dyslipidemia etiology.**

**Secondary hyperlipidemia:** refers to dyslipidemia caused by other diseases. The main diseases that can cause dyslipidemia are: obesity, diabetes mellitus, nephrotic syndrome, hypothyroidism, renal failure, liver disease, systemic lupus erythematosus, glycogen accumulation, myeloma, lipodystrophy, acute porphyria, polycystic ovary syndrome, etc. In addition, certain drugs such as diuretics, non-cardioselective beta-blockers, and glucocorticoids may also lead to secondary dyslipidemia.

**Primary hyperlipidemia**: In addition to poor lifestyle (e.g., high energy, high fat and high sugar diet, excessive alcohol consumption, etc.) associated with dyslipidemia, most primary hyperlipidemia is due to a single gene or multiple gene mutations. Because hyperlipidemia due to genetic mutations is mostly familial and has a clear genetic predisposition, especially in those with a single genetic mutation, it is often clinically referred to as familial hyperlipidemia.

# Dyslipidemia

**Clinical classification of dyslipidemia**

| | TC | TG | HDL-C | Equivalent to WHO phenotype |
|---|---|---|---|---|
| Hypercholesteremia | Increase | | | Ⅱa |
| HTG | | Increase | | Ⅳ、Ⅰ |
| Mixed hyperlipidemia | Increase | Increase | | Ⅱb, Ⅲ, Ⅳ, Ⅴ |
| Low HDL-C | | | Reduce | |

# Appropriate lipid levels and abnormal cut points

Appropriate lipid levels and abnormal stratification criteria for ASCVD primary prevention population in China [mmol/L(mg/dl)

| Stratification | TC | LDL-C | HDL-C | Non -HDL-C | TG |
|---|---|---|---|---|---|
| Ideal level | | < 2.6 (100) | | < 3.4 (130) | |
| Appropriate level | < 5.2 (200 ) | < 3.4 (130) | | < 4.1 (160) | < 1.7 (150) |
| Marginal Elevation | ⩾ 5.2 (200) and <6.2 (240) | ⩾ 3.4 (130) and <4.1 (160) | | ⩾ 4.1 (160) and <4.9 (190) | ⩾ 1.7 (150) and <2.3 (200) |
| Elevation | ⩾ 6.2 (240) | ⩾ 4.1 (160) | | ⩾ 4.9 (190) | ⩾ 2.3 (200) |
| Reduce | | | < 1.0 (40) | | |

Appropriate levels of lipids and abnormal cut points are primarily applicable to the target Population of ASCVD primary prevention.

Note: ASCVD: atherosclerotic cardiovascular disease; TC; total

# People who need to focus on blood lipid levels

Patients with ASCVD are at very-high risk for ASCVD if they have the following, particular focus on lipid levels is recommended[2]:

- Recurrent ASCVD events
- Multiple coronary artery lesions
- Recent ACS
- Atherosclerotic cardiovascular disease of the heart, brain, or peripheral vessels
- LDL-C ≥ 4.9 mmol/L

## 1 Past History of ASCVD[1]

**e.g.: CAD, stroke and other atherosclerotic diseases**

## 2 Familial History of CAD of Hyperlipidemia [1]

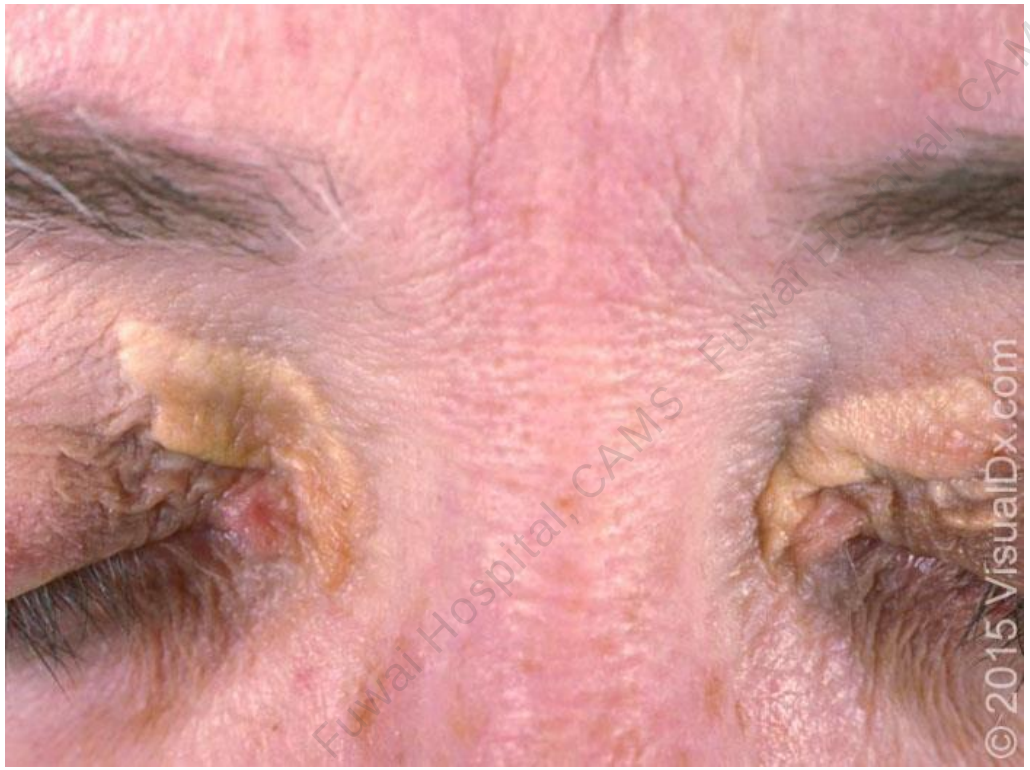
- **Family history of hyperlipidemia**
- **Father or brothers with ischemic CVD before 55**
- **Mother or sister with ischemic CVD before 65**

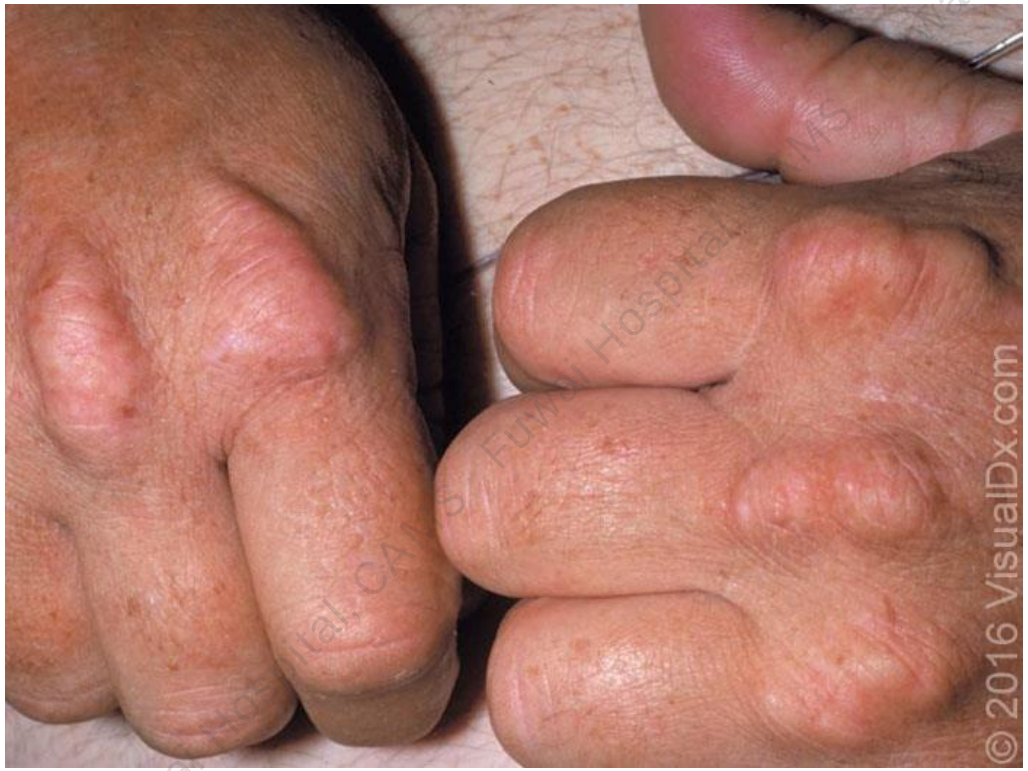
## 3 Factors predisposing to dyslipidemia[1]

**Hypertension, diabetes, obesity, smoking, etc.**

## 4 Cutaneous/tendinous xanthomas[1]

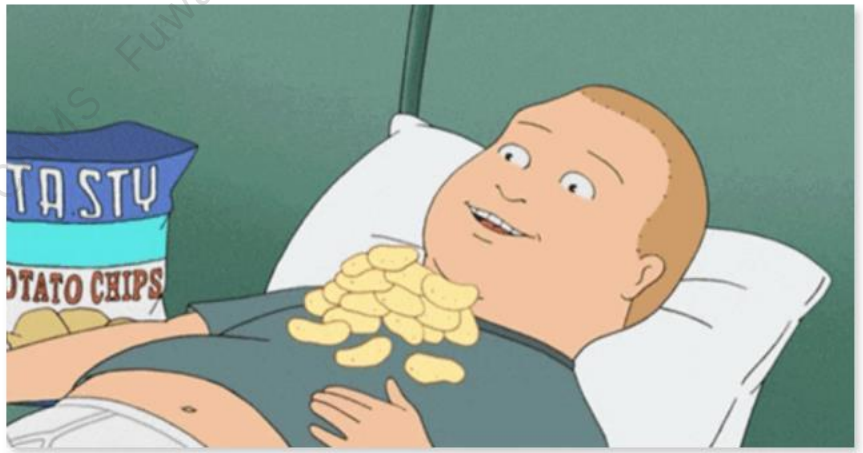
# Cutaneous/tendinous xanthomas



# Factors affecting blood lipids: modifiable

Some of the factors that affect blood lipid levels can be changed, such as diet, weight, and exercise.



# Factors affecting blood lipids: unchangeable

Other factors that affect lipid levels are beyond our power to change, such as age and gender, genetic factors

# Intervention for hyperlipidemia

Quit Smoking


Balanced Diet

Excercise


Weight Control

Medication

If dyslipidemia has occurred, regardless of the severity and whether or not medication is required, **lifestyle interventions should be started immediately** and maintained long after lipids have returned to normal to avoid rebound of lipid levels.

# Summary

- Dyslipidemia is a serious risk to human health
- "Bad" cholesterol (LDL-C) is one of the ultimate culprit of coronary heart disease and a key indicator for controlling blood lipids

# Thank you!