S.I.Te.C.S.

SOCIETÀ ITALIANA DI TERAPIA CLINICA E SPERIMENTALE

DYSLIPIDAEMIAS: PRESENT AND FUTURE APPROACHES TO PHARMACOLOGICAL INTERVENTION

November 9th-10th, Sorrento (NA) - Italy

Clinical cases

A low-risk subject with elevated LDL-C

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♂ **47-y**

- **FAMILY HISTORY:**
  - mother 73-y: LDL-C 106 mg/dL with SIMVA 20 mg/d
  - father 79-y: ischemic stroke at 78-y, on ATORVA 10 mg/d
  - 2 healthy brothers
  - sister 53-y: LDL-C 144 mg/dL, otherwise healthy
  - 2 healthy sons

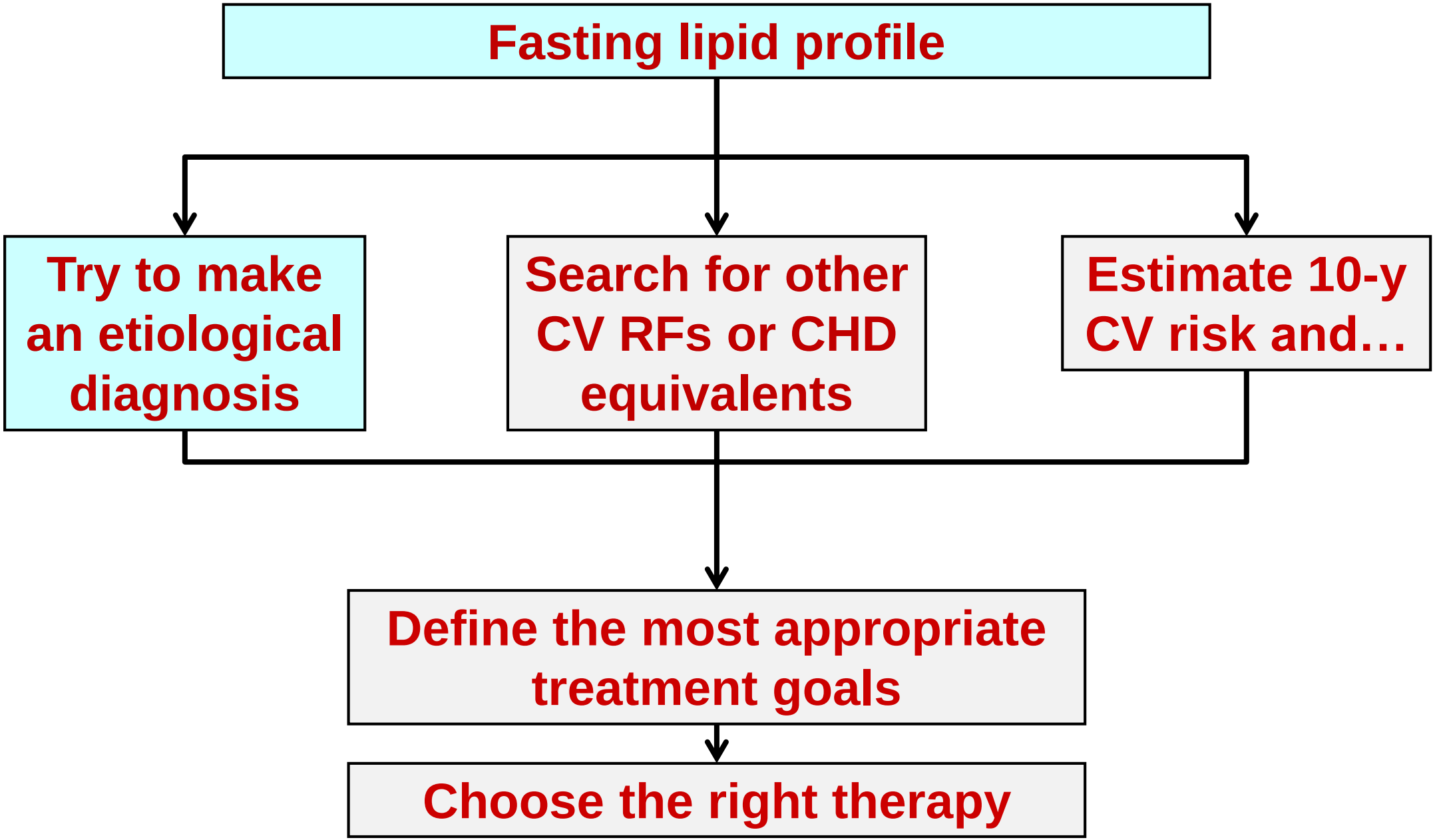
- **PERSONAL CLINICAL HISTORY:**
  - Recent diagnosis of hypertension (no drug therapy)

- **PATIENT CHARACTERISTICS:**
  - non smoker
  - BP 140/90 mmHg, without LVH
  - Weight/Height 81-Kg/170 cm; BMI 28; WC102 cm
  - No evidence of xanthomas, arcus cornealis

- 1-y before current visit:	TC	261	mg/dl
	TGs	293	mg/dl
	LDL-C	153	mg/dl
	HDL-C	49	mg/dl
	FPG	92	mg/dl

Therapeutic Lifestyle Changes

- Current visit:	TC	239	mg/dl
	TGs	206	mg/dl
	LDL-C	148	mg/dl
	HDL-C	50	mg/dl
	FPG	89	mg/dl


Fasting lipid profile
Try to make an etiological diagnosis
Search for other CV RFs or CHD equivalents
Estimate 10-y CV risk and…
Define the most appropriate treatment goals
Choose the right therapy

More frequent of dyslipidemias

Primitive Dyslipidemia		Secondary dyslipidemias
- Polygenic HC LDL-C>140-190 mg/dl (not FH criteria)	YES	NO Hypothyroidism Paraproteinemia
- FCH LDL-C>160 mg/dl and/or TG >200 mg/dl	NO	NO Cholestatic liver disease Nephrotic syndrome
- FH LDL-C>190 mg/dl	NO	NO CKD Nervous anorexia
- Dysbetalipoproteinemia CT >300 mg/dl and TG >300 mg/dl (TC/TG ~ 0.5-1)	NO	NO Drugs Alcohol
- Familial HTG TG >800 mg/dl		YES Obesity, Overweight (+)
- Other…	NO	NO DM

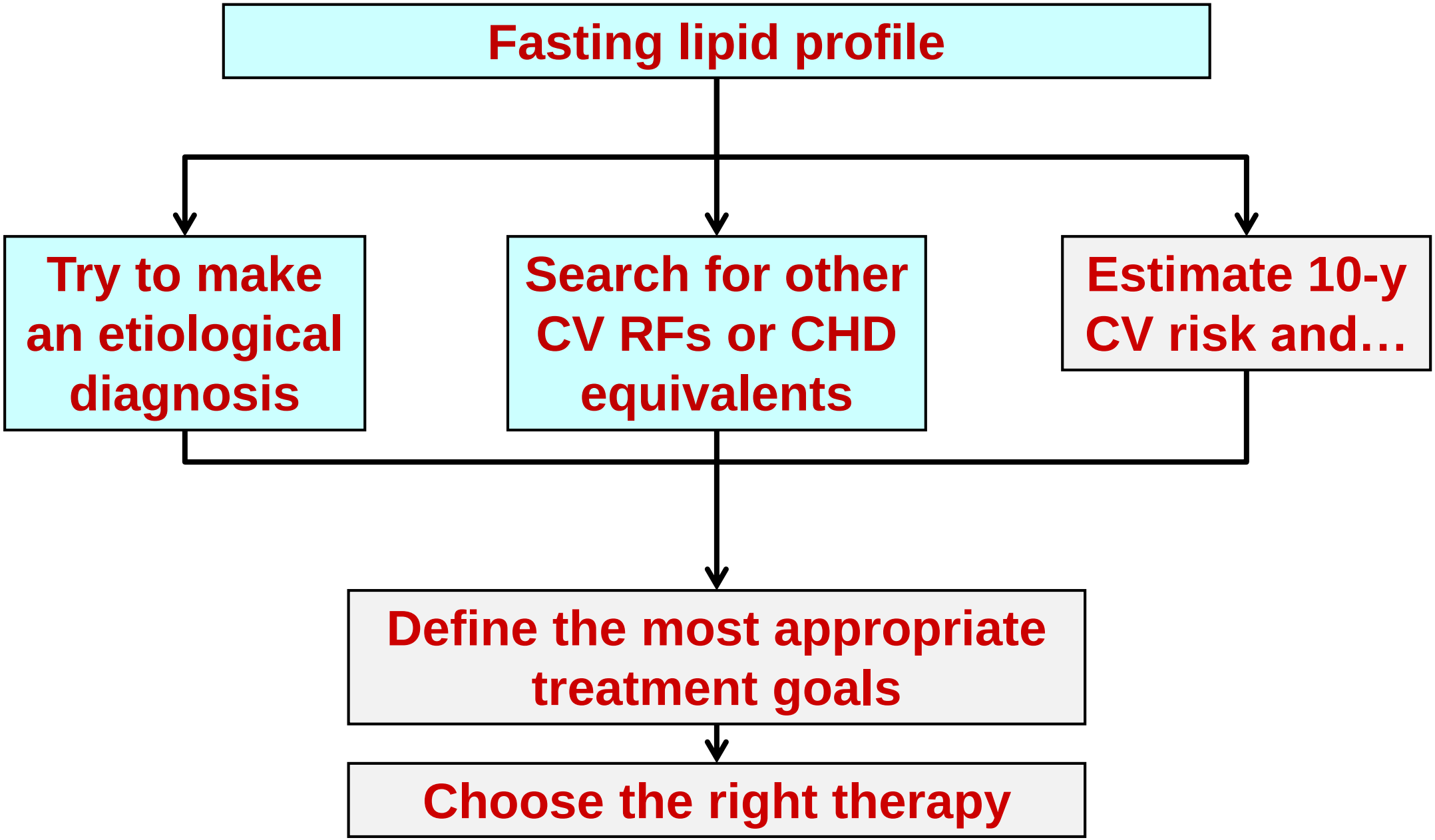
hypercholesterolemia
hypertriglyceridemia

Diagnosis of HeFH (*Dutch Lipid Clinic Network Score*)

Criteria			Score	Patient Score
Family history				
First degree relative with known premature coronary and/or vascular disease (men aged <55 years, women aged <60 years) OR First degree relative with known LDL-cholesterol above the 95th percentile for age and gender		190 mg/dL	1	
First degree relative with tendinous xanthomata and/or arcus cornealis OR Children aged <18 years with LDL-cholesterol above the 95th percentile for age and gender		155 mg/dL	2	
Clinical history				
Patients with premature coronary artery disease (men aged <55 years, women aged <60 years)			2	
Patients with premature cerebral or peripheral vascular disease (men aged <55 years, women aged <60 years)			1	
Physical examination				
Tendinous xanthomata			6	
Arcus cornealis before 45 years of age			4	
Investigation				
LDL-cholesterol (mmol/L)	LDL-C ≥8.5	>325 mg/dL	8	
NB. This is the **untreated** LDL-cholesterol concentration. See supporting documentation for method of calculation.	LDL-C 6.5–8.4	251-325 mg/dL	5	
	LDL-C 5.0–6.4	191-250 mg/dL	3	
	LDL-C 4.0–4.9	155-190 mg/dL	1	
			Patient total	

Diagnosis	Total	
Definite FH	>8	OR x13
Probable FH	6-8	
Possible FH	3-5	OR x5
Unlikely FH	<3	OR x1

Causative mutation (LDLR, ApoB, PCSK9): score 8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Main CV risk factors

Age male >45 years
female >55 years

Family history of premature CHD (< 55 years in male first-degree relatives, or <65 years of age in female first degree relatives)

Current cigarette smoking

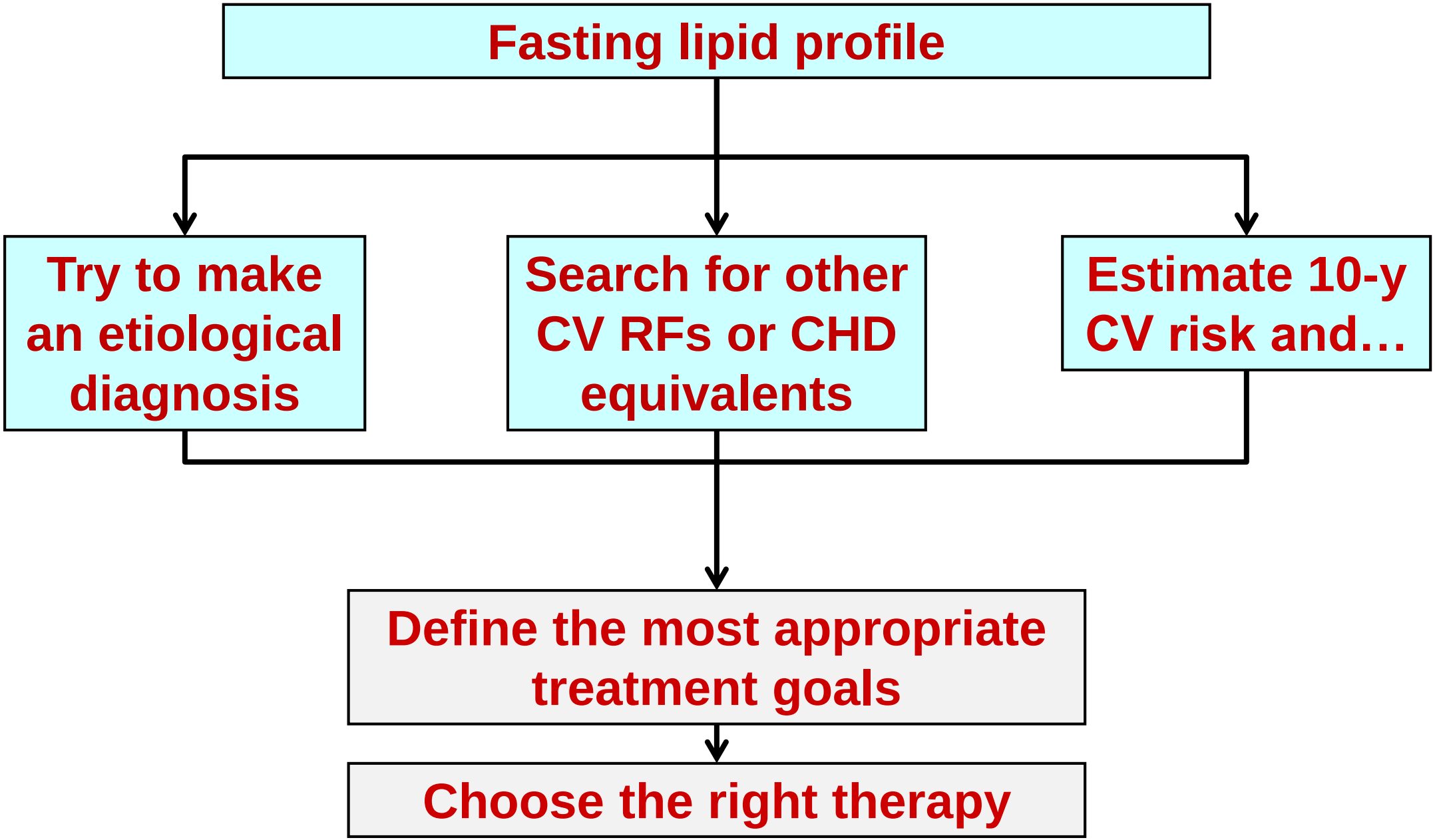
Hypertension (>140/90 mmHg or on anti-hypertensive medication)

Low HDL cholesterol (<40 mg/dl in men and <50 mg/dl in women)

Negative (protector) risk factor: HDL cholesterol > 60mg dl

CV High Risk Equivalents

CHD, CVD, PAD, AAA	➡ NO
CKD	➡ NO
Diabetes	➡ NO
FH	➡ NO
Very high level of individual RFs	➡ NO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Cardiovascular risk estimation

Low-risk regions of Europe

Age	Systolic blood pressure (mmHg)	WOMEN Non-smoker 4	5	6	7	WOMEN Smoker 4	5	6	7	MEN Non-smoker 4	5	6	7	MEN Smoker 4	5	6	7
70	180	7	8	8	9	11	11	12	13	12	14	15	17	18	20	22	24
	160	6	6	7	7	9	9	10	11	10	11	13	14	15	16	18	20
	140	5	5	6	6	7	8	8	9	8	9	10	12	12	13	15	17
	120	4	4	5	5	6	6	7	7	7	8	9	10	10	11	12	14
65	180	4	4	5	5	7	7	8	9	8	9	10	12	12	14	16	18
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	120	2	2	2	2	3	3	3	4	3	4	5	5	5	6	7	8
60	180	2	3	3	3	4	5	5	6	5	6	7	8	8	10	11	13
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	140	1	1	1	2	2	2	3	3	3	3	3	4	4	5	6	7
	120	1	1	1	1	2	2	2	2	2	2	2	3	3	4	4	5
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	160	1	1	1	1	2	2	2	3	2	2	3	3	4	4	5	6
	140	1	1	1	1	1	1	1	2	1	2	2	2	3	3	3	4
	120	0	0	0	1	1	1	1	1	1	1	1	2	2	2	2	3
50	180	1	1	1	1	2	2	2	3	2	2	3	3	4	5	5	6
	160	0	0	1	1	1	1	1	2	1	1	2	2	2	3	3	4
	140	0	0	0	0	1	1	1	1	1	1	1	1	1	2	2	3
	120	0	0	0	0	0	0	0	1	0	1	1	1	1	1	1	2
40	180	0	0	0	0	1	1	1	1	1	1	1	1	2	2	3	3
	160	0	0	0	0	0	0	0	1	0	0	1	1	1	1	1	2
	140	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1
	120	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1

Total cholesterol (mmol/L)

<3% 3-4% 5-9% ≥10%

Cardiovascular risk estimation

10-y CV risk: 0-1%

Low-risk regions of Europe

Age	Systolic blood pressure (mmHg)	WOMEN Non-smoker				WOMEN Smoker				MEN Non-smoker				MEN Smoker			
		4	5	6	7	4	5	6	7	4	5	6	7	4	5	6	7
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	120	1	1	1	1	2	2	2	2	2	2	2	3	3	4	4	5
55	180	1	1	2	2	3	3	3	4	3	4	4	5	6	7	8	9
	160	1	1	1	1	2	2	2	3	2	2	3	3	4	4	5	6
	140	1	1	1	1	1	1	1	2	1	2	2	2	3	3	3	4
	120	0	0	0	1	1	1	1	1	1	1	1	2	2	2	2	3
50	180	1	1	1	1	2	2	2	3	2	2	3	3	4	5	5	6
	160	0	0	1	1	1	1	1	2	1	1	2	2	2	3	3	4
	140	0	0	0	0	1	1	1	1	1	1	1	1	1	2	2	3
	120	0	0	0	0	0	0	0	1	0	1	1	1	1	1	1	2
40	180	0	0	0	0	1	1	1	1	1	1	1	1	2	2	3	3
	160	0	0	0	0	0	0	0	1	0	0	1	1	1	1	1	2
	140	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1
	120	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1

Total cholesterol (mmol/L)

<3% | 3-4% | 5-9% | ≥10%

Cardiovascular risk estimation

10-y CV risk: 0-1%

RR: x2

Low-risk regions of Europe

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	160	2	2	2	2	3	3	4	4	4	4	5	5	6	7	8	9
	140	1	1	1	2	2	2	3	3	3	3	3	4	4	5	6	7
	120	1	1	1	1	2	2	2	2	2	2	2	3	3	4	4	5
55	180	1	1	2	2	3	3	3	4	3	4	4	5	6	7	8	9
	160	1	1	1	1	2	2	2	3	2	2	3	3	4	4	5	6
	140	1	1	1	1	1	1	1	2	1	2	2	2	3	3	3	4
	120	0	0	0	1	1	1	1	1	1	1	1	2	2	2	2	3
50	180	1	1	1	1	2	2	2	3	2	2	3	3	4	5	5	6
	160	0	0	1	1	1	1	1	2	1	1	2	2	2	3	3	4
	140	0	0	0	0	1	1	1	1	1	1	1	1	1	2	2	3
	120	0	0	0	0	0	0	0	1	0	1	1	1	1	1	1	2
40	180	0	0	0	0	1	1	1	1	1	1	1	1	2	2	3	3
	160	0	0	0	0	0	0	0	1	0	0	1	1	1	1	1	2
	140	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1
	120	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1

Total cholesterol (mmol/L)

<3% 3-4% 5-9% ≥10%

Systolic blood pressure (mmHg)	Non-smoker 4	5	6	7	8	Smoker 4	5	6	7	8
180	3	3	4	5	6	6	7	8	10	12
160	2	3	3	4	4	4	5	6	7	8
140	1	2	2	2	3	3	3	4	5	6
120	1	1	1	2	2	2	2	3	3	4

Cholesterol (mmol/L)

Cardiovascular risk estimation

CV risk age: 55-y

10-y CV risk: 0-1%

RR: x2

Low-risk regions of Europe

Systolic blood pressure (mmHg)	WOMEN Non-smoker				WOMEN Smoker				Age	MEN Non-smoker				MEN Smoker			
	4	5	6	7	4	5	6	7		4	5	6	7	4	5	6	7
180	7	8	8	9	11	11	12	13	70	12	14	15	17	18	20	22	24
160	6	6	7	7	9	9	10	11		10	11	13	14	15	16	18	20
140	5	5	6	6	7	8	8	9		8	9	10	12	12	13	15	17
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180	2	3	3	3	4	5	5	6	60	5	6	7	8	8	10	11	13
160	2	2	2	2	3	3	4	4		4	4	5	5	6	7	8	9
140	1	1	1	2	2	2	3	3		3	3	3	4	4	5	6	7
120	1	1	1	1	2	2	2	2		2	2	2	3	3	4	4	5
180	1	1	2	2	3	3	3	4	55	3	4	4	5	6	7	8	9
160	1	1	1	1	2	2	2	3		2	2	3	3	4	4	5	6
140	1	1	1	1	1	1	1	2		1	2	2	2	3	3	3	4
120	0	0	0	1	1	1	1	1		1	1	1	2	2	2	2	3
180	1	1	1	1	2	2	2	3	50	2	2	3	3	4	5	5	6
160	0	0	1	1	1	1	1	2		1	1	2	2	2	3	3	4
140	0	0	0	0	1	1	1	1		1	1	1	1	1	2	2	3
120	0	0	0	0	0	0	0	1		0	1	1	1	1	1	1	2
180	0	0	0	0	1	1	1	1	40	1	1	1	1	2	2	3	3
160	0	0	0	0	0	0	0	1		0	0	1	1	1	1	1	2
140	0	0	0	0	0	0	0	0		0	0	0	0	1	1	1	1
120	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	1

Total cholesterol (mmol/L)

<3% | 3-4% | 5-9% | ≥10%

Systolic blood pressure (mmHg)	Non-smoker 4	5	6	7	8	Smoker 4	5	6	7	8
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140	1	2	2	2	3	3	3	4	5	6
120	1	1	1	2	2	2	2	3	3	4

Cholesterol (mmol/L)

Lifetime CV risk

Inputs

Sex: **Male**
Age: **48**
Race: **White**

Total Cholesterol: **239** mg/dL
HDL-Cholesterol: **50** mg/dL
Systolic Blood Pressure: **140** mm Hg

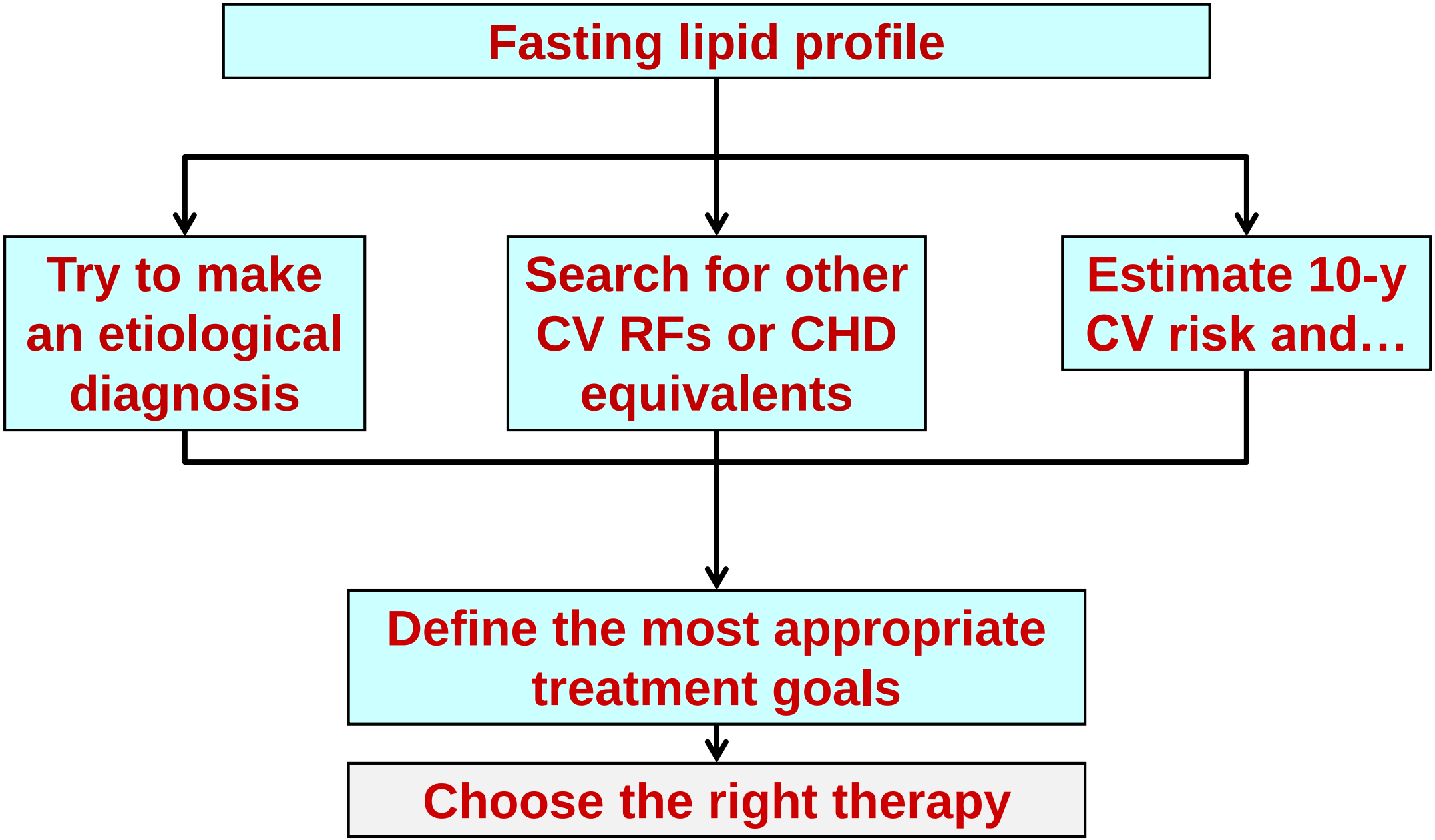
Diabetes: **No**
Smoker: **No**
Treatment for Hypertension: **No**

Lifetime ASCVD Risk

46% calculated risk

5% risk with optimal risk factors

Optimal risk factors include: Total cholesterol of ≤ 170 mg/dL (4.40 mmol/L), HDL-cholesterol of ≥ 50 mg/dL (1.30 mmol/L), Systolic BP of ≤ 110 mm Hg, Not taking medications for hypertension, Not a diabetic, Not a smoker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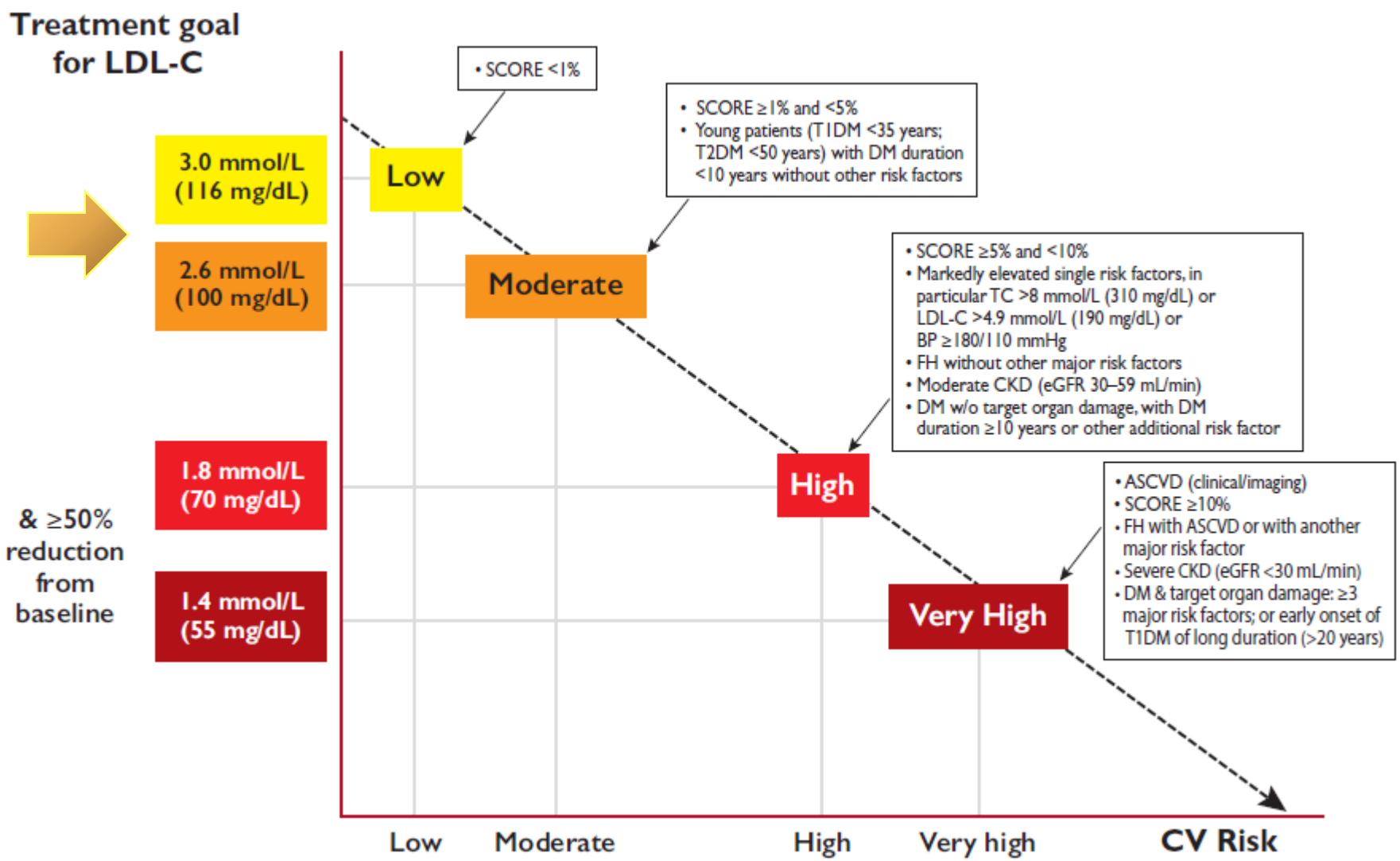
LDL-C treatment goals



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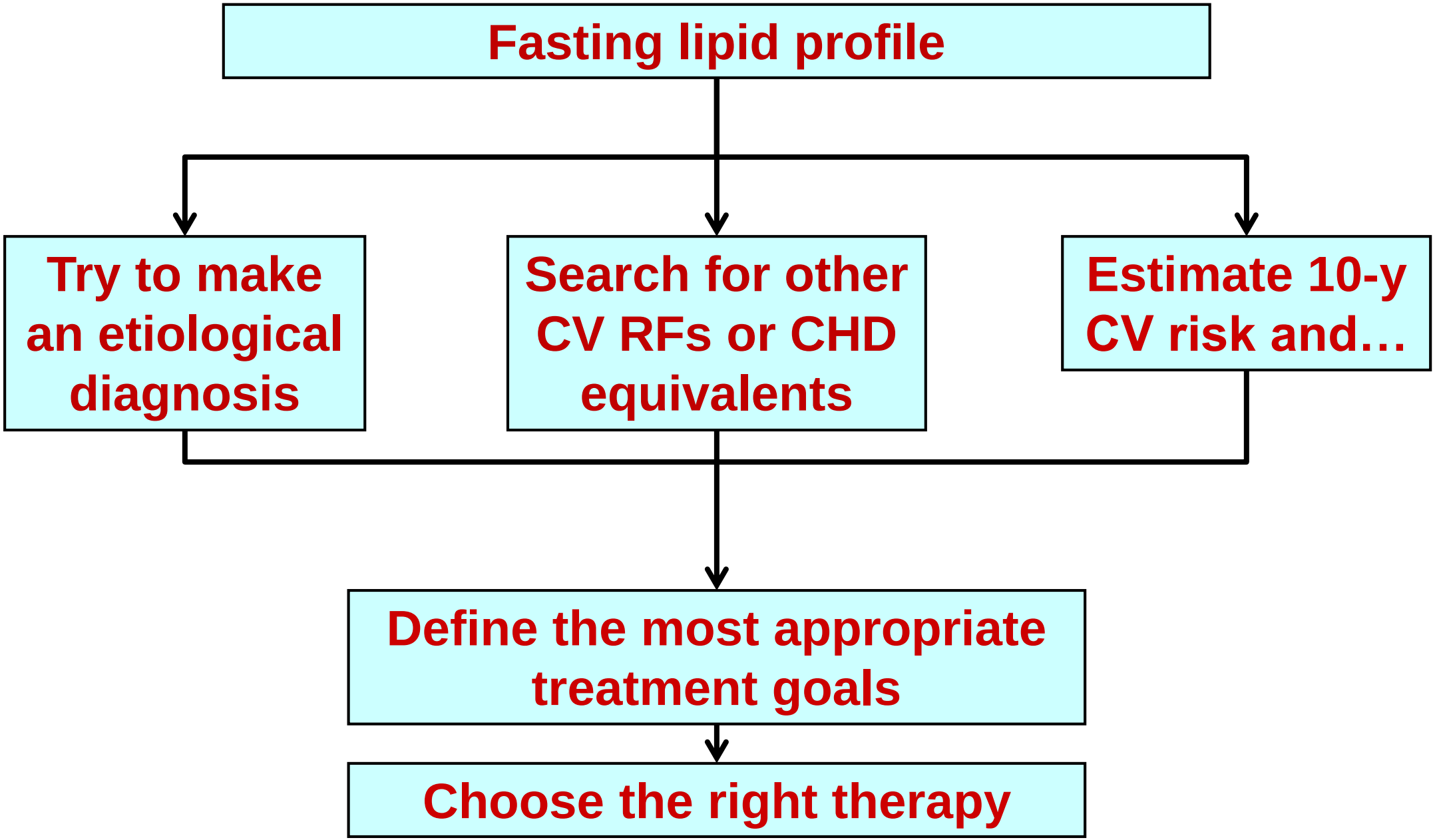
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Starting Fasting Lipid Profile

TC	239	mg/dl
TGs	206	mg/dl
LDL-C	148	mg/dl
HDL-C	50	mg/dl

LDL-C treatment goals

Low-risk : <116 mg/dL

Moderate-risk : <100 mg/dL

Requested % LDL-C reduction to reach the goals

Low-risk: 148 – 115 = 33 mg/dL….33/162 = > -22%

Moderate-risk: 148 – 99 = 49 mg/dL….49/162= > -33%

Starting Fasting Lipid Profile

TC	239	mg/dl		
TGs	206	mg/dl		
LDL-C	148	mg/dl		
HDL-C	50	mg/dl	non-HDL-C	189 mg/dL

Treatment

TLC + Nutraceutical combination (low-dose RYR + BBR)

4-month visit + FLP

Weight	77 Kg
BMI	26.6
WC	97 cm
BP	135/80 mmHg

TC	194 mg/dln	(-19%)
TGs	157 mg/dl	(-23%)
LDL-C	112 mg/dl	(-24%)
HDL-C	51 mg/dl	
non-HDL-C	143 mg/dL	(-24%)

Why has this therapeutic choice been preferred ?

Total CV risk (SCORE) %	LDL-C levels				
	<70 mg/dL <1.8 mmol/L	70 to <100 mg/dL 1.8 to <2.6 mmol/L	100 to <155 mg/dL 2.6 to <4.0 mmol/L	155 to <190 mg/dL 4.0 to <4.9 mmol/L	≥190 mg/dL ≥4.9 mmol/L
<1	No lipid intervention	No lipid intervention	No lipid intervention	No lipid intervention	Lifestyle intervention, consider drug if uncontrolled

	Total CV risk (SCORE) %	Untreated LDL-C levels					
		<1.4 mmol/L (55 mg/dL)	1.4 to <1.8 mmol/L (55 to <70 mg/dL)	1.8 to <2.6 mmol/L (70 to <100 mg/dL)	2.6 to <3.0 mmol/L (100 to <116 mg/dL)	3.0 to <4.9 mmol/L (116 to <190 mg/dL)	≥4.9 mmol/L (≥190 mg/dL)
Primary prevention	<1, low-risk	Lifestyle advice	Lifestyle advice	Lifestyle advice	Lifestyle advice	Lifestyle intervention, consider adding drug if uncontrolled	Lifestyle intervention and concomitant drug intervention
	Class[a]/Level[b]	I/C	I/C	I/C	I/C	IIa/A	IIa/A
	≥1 to <5, or moderate risk (see *Table* 4)	Lifestyle advice	Lifestyle advice	Lifestyle advice	Lifestyle intervention, consider adding drug if uncontrolled	Lifestyle intervention, consider adding drug if uncontrolled	Lifestyle intervention and concomitant drug intervention

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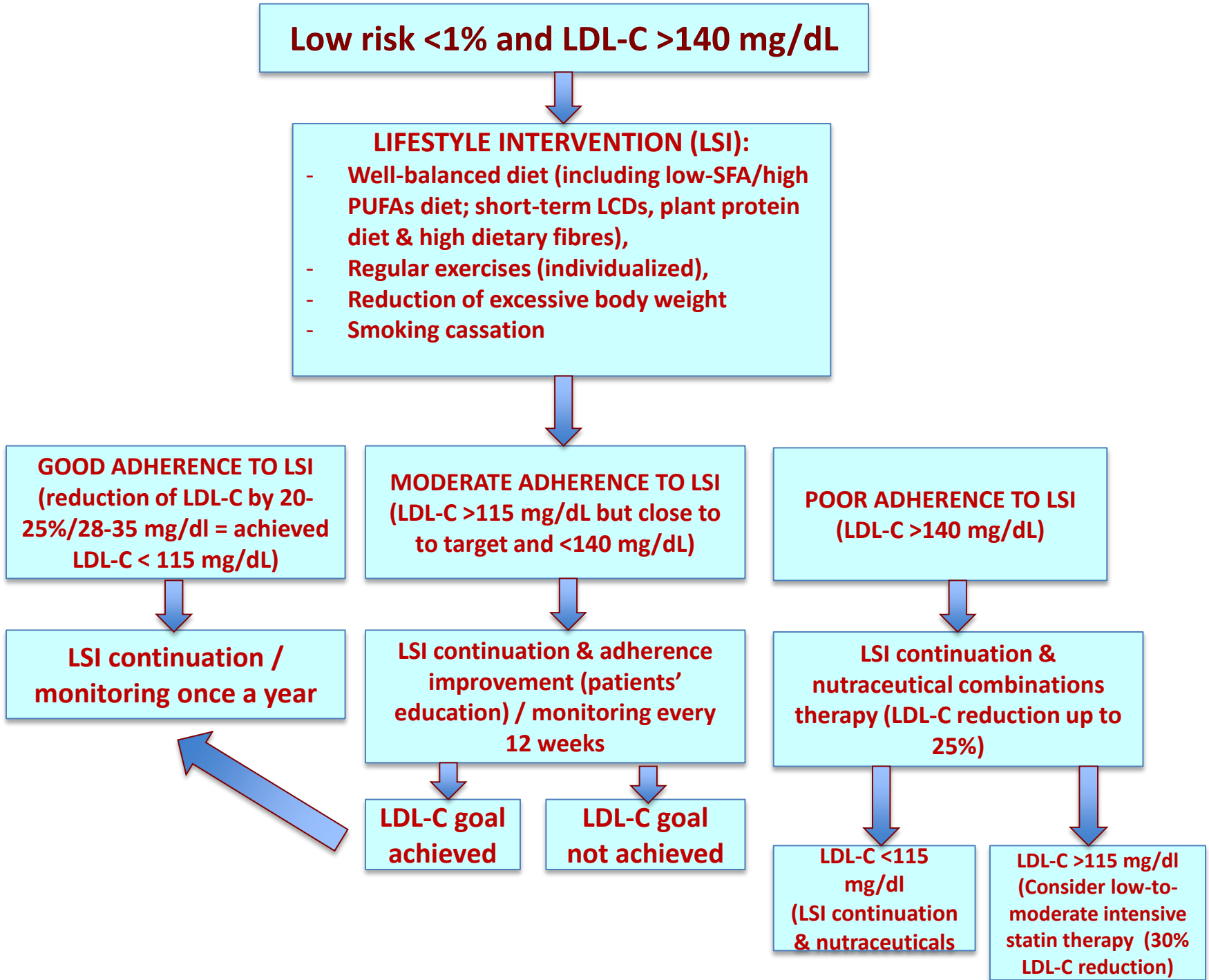
Low risk <1% and LDL-C >140 mg/dL
LIFESTYLE INTERVENTION (LSI):
- Well-balanced diet (including low-SFA/high PUFAs diet; short-term LCDs, plant protein diet & high dietary fibres),
- Regular exercises (individualized),
- Reduction of excessive body weight
- Smoking cassation
GOOD ADHERENCE TO LSI (reduction of LDL-C by 20-25%/28-35 mg/dl = achieved LDL-C < 115 mg/dL)
MODERATE ADHERENCE TO LSI (LDL-C >115 mg/dL but close to to target and <140 mg/dL)
POOR ADHERENCE TO LSI (LDL-C >140 mg/dL)
LSI continuation / monitoring once a year
LSI continuation & adherence improvement (patients' education) / monitoring every 12 weeks
LSI continuation & nutraceutical combinations therapy (LDL-C reduction up to 25%)
LDL-C goal achieved
LDL-C goal not achieved
LDL-C <115 mg/dl (LSI continuation & nutraceuticals
LDL-C >115 mg/dl (Consider low-to-moderate intensive statin therapy (30% LDL-C reduction)