時間：九十九年六月十三日

新陳代謝症候群與三高

演講人：楊仕山 醫師

新陳代謝症候群台灣版黃金標準

診斷標準： **5** 個危險因子大於等於 **3** 個

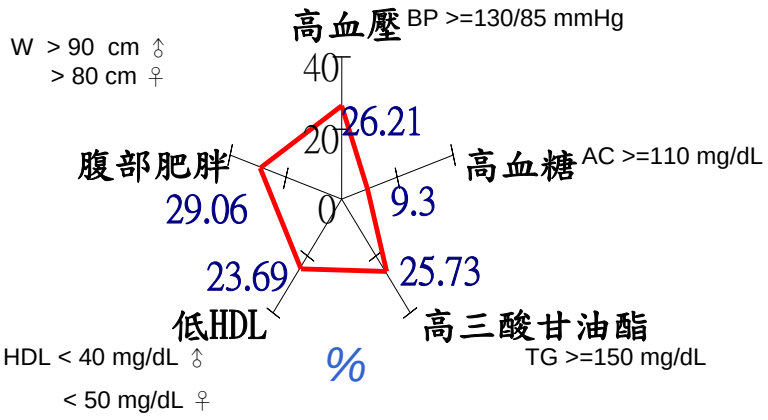
危險因子	定義範圍
腹部肥胖 (腰圍)	
男	>90 cm
女	>80 cm
三酸甘油酯	≥150 mg/dL
HDL-C 男	<40 mg/dL
女	<50 mg/dL
血壓	≥130/≥85 mm Hg
空腹血糖	≥110 mg/dL

新陳代謝症候群(MetS)

同義字

- 胰島素阻抗症候群(Insulin resistance syndrome,IRS)
- X 症候群　(Syndrome X)
- 代謝不良症候群(Dysmetabolic syndrome)
- 多發性新陳代謝症候群 (Multiple metabolic syndrome)

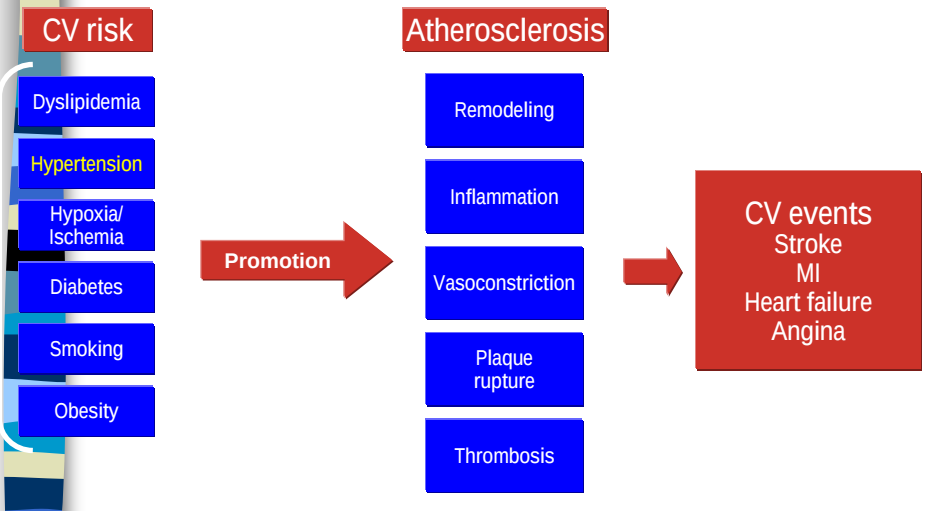
新陳代謝症候群:台灣盛行率2004



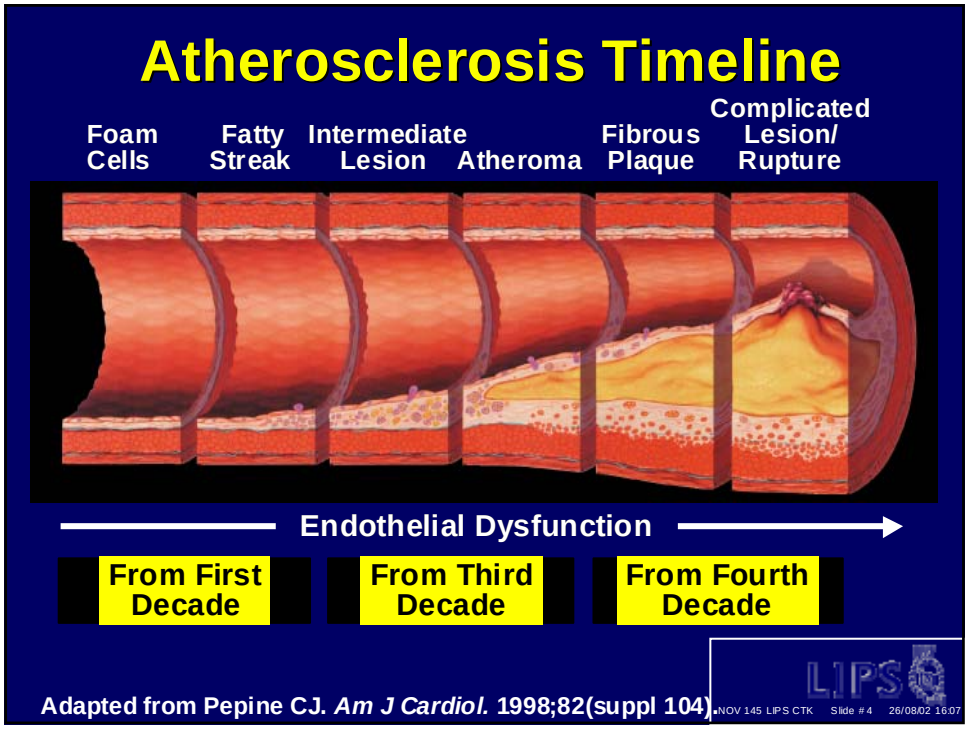
新陳代謝症候群個案的主要成份組

	人數	佔新陳代謝症候群個案(1023)之百分比
新陳代謝症候群	**1023**	**100%**
肥胖	**852**	**83.3%**
肥胖+高三酸甘油酯症	**696**	**68.04%**
肥胖+高三酸甘油酯症+高血壓	**457**	**44.67%**
肥胖+高三酸甘油酯症+高血壓+低的高密度膽固醇	**232**	**22.68%**

Risk factors are part of the same atherosclerotic disease process



Adapted from Schiffrin EL, et al. *Am J Hypertens* 2002;15:115s-122s.


Atherosclerosis Timeline
Foam Cells
Fatty Streak
Intermediate Lesion
Atheroma
Fibrous Plaque
Complicated Lesion/ Rupture
Endothelial Dysfunction
From First Decade
From Third Decade
From Fourth Decade
Adapted from Pepine CJ. Am J Cardiol. 1998;82(suppl 104)
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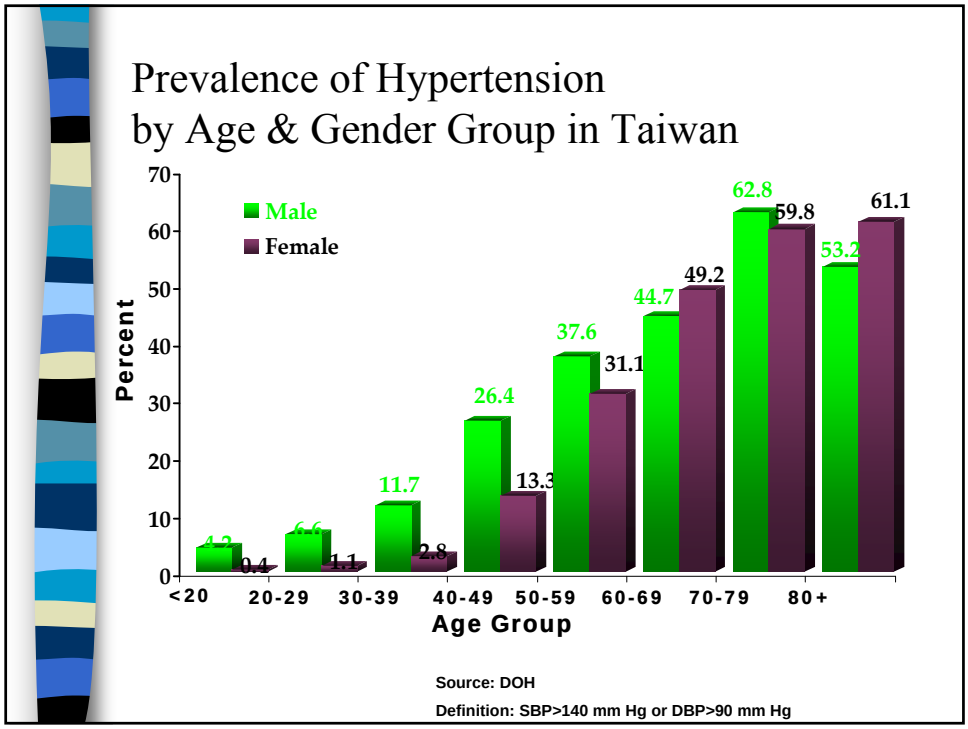
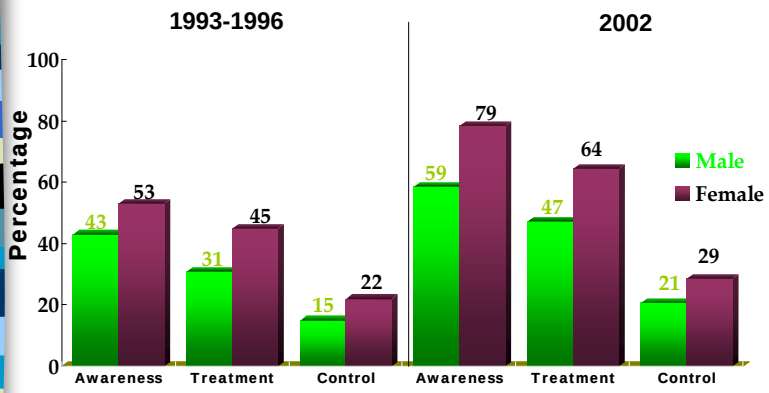
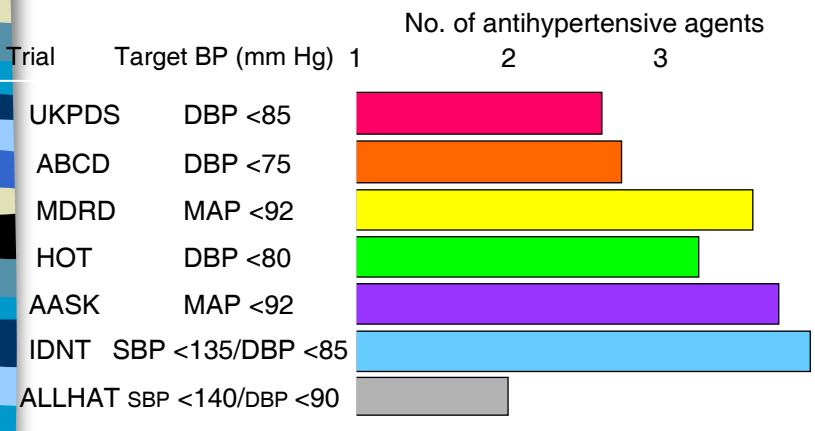

Prevalence of Hypertension
by Age & Gender Group in Taiwan
Male
Female
Percent
70
60
50
40
30
20
10
0
4.3
0.4
6.6
1.1
11.7
2.8
26.4
13.3
37.6
31.1
44.7
49.2
62.8
59.8
53.2
61.1
<20
20-29
30-39
40-49
50-59
60-69
70-79
80+
Age Group
Source: DOH
Definition: SBP>140 mm Hg or DBP>90 mm Hg

Awareness, Treatment and Control Rate of Hypertension in Taiwan

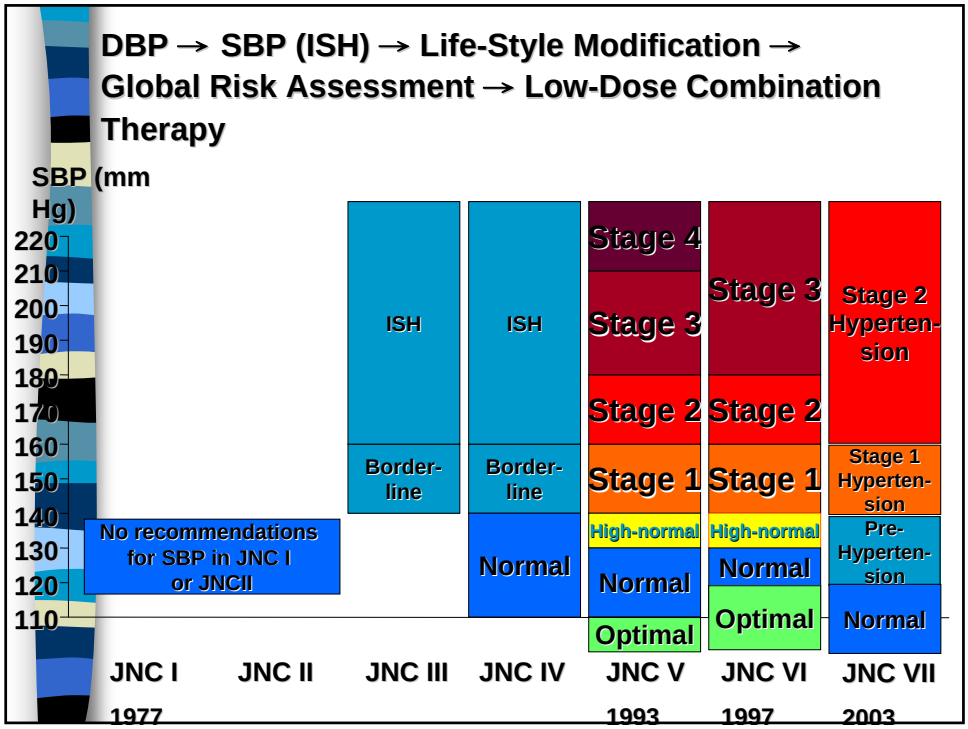


Multiple Antihypertensive Agents Are Needed to Achieve Target BP



DBP, diastolic blood pressure; MAP, mean arterial pressure; SBP, systolic blood pressure.

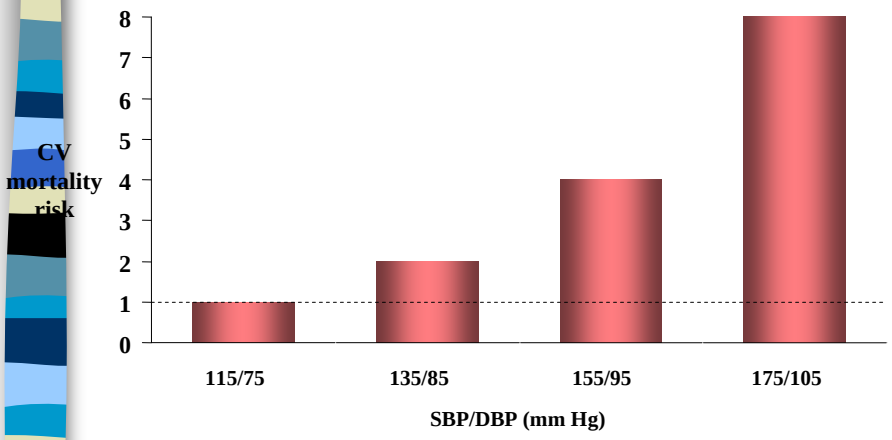
Bakris GL et al. *Am J Kidney Dis.* 2000;36:646-661.
Lewis EJ et al. *N Engl J Med.* 2001;345:851-860.
Cushman WC et al. *J Clin Hypertens*. 2002;4:393-404.



2007 ESH/ESC , 2009 JSH

category	Systolic BP (mmHg)		Diastolic BP (mmHg)
Optimal BP	< 120	&	< 80
Normal BP	< 130	&	< 85
High normal BP	130-139	or	85-89
Grade 1 HTN	140-159	or	90-99
Grade 2 HTN	160-179	or	100-109
Grade 3 HTN	≧180	or	≧110
Isolated systolic HTN	≧140	&	< 90

CV Mortality Risk Doubles with Each 20/10 mm Hg BP Increment*

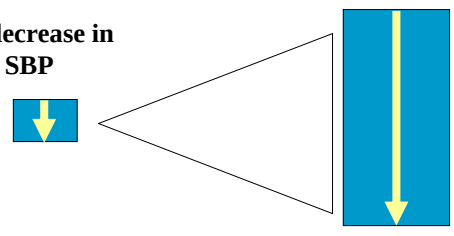


*Individuals aged 40-70 years, starting at BP 115/75 mm Hg.
Lewington S, et al. *Lancet.* 2002; 60:1903-1913.
JNC 7. *JAMA.* 2003;289:2560-2572.

BP Reductions as Little as 2 mm Hg Reduce the Risk of CV Events by Up to 10%

- **Meta-analysis of 61 prospective, observational studies**
- **1 million adults**
- **12.7 million person-years**

2 mm Hg decrease in mean SBP



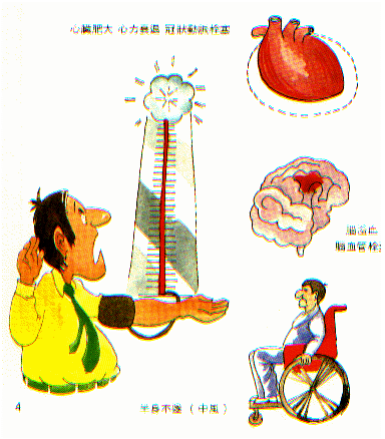
7% reduction in risk of ischemic heart disease mortality

10% reduction in risk of stroke mortality

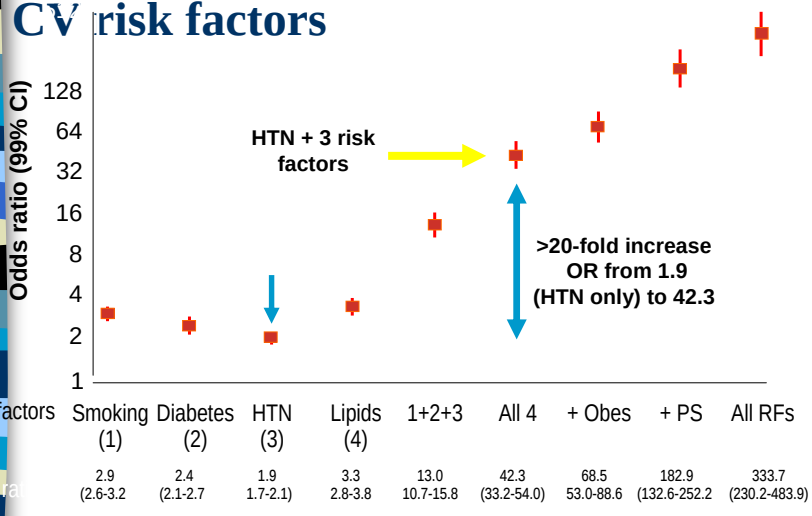
Lewington S et al. *Lancet* 2002;360:1903-1913.

高血壓的併發症

- 腦中風
- 心肌梗塞
- 心衰竭
- 腎衰竭
- 視網膜出血

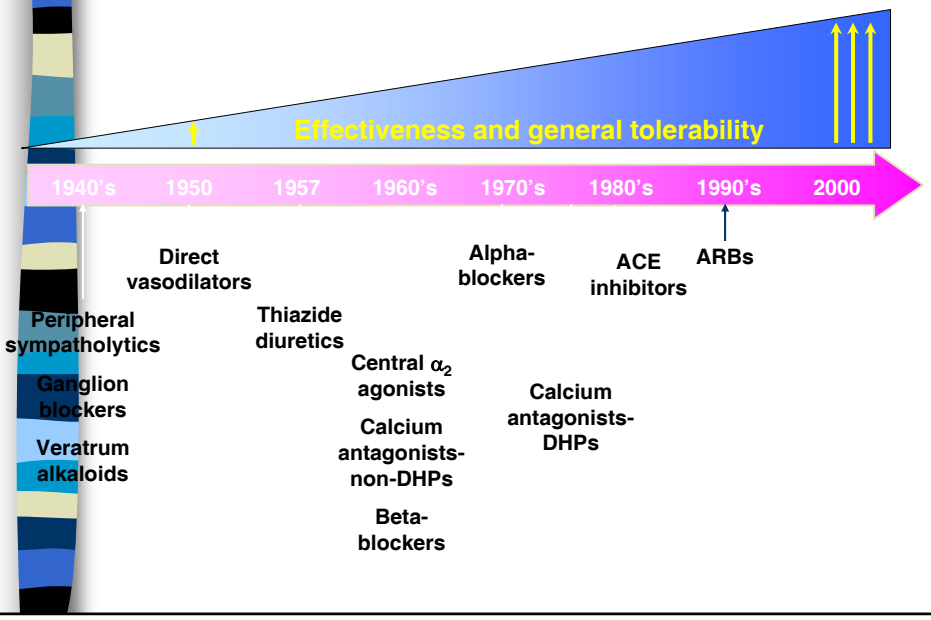


Increased number of CV events (MI) in patients with hypertension plus other CV risk factors

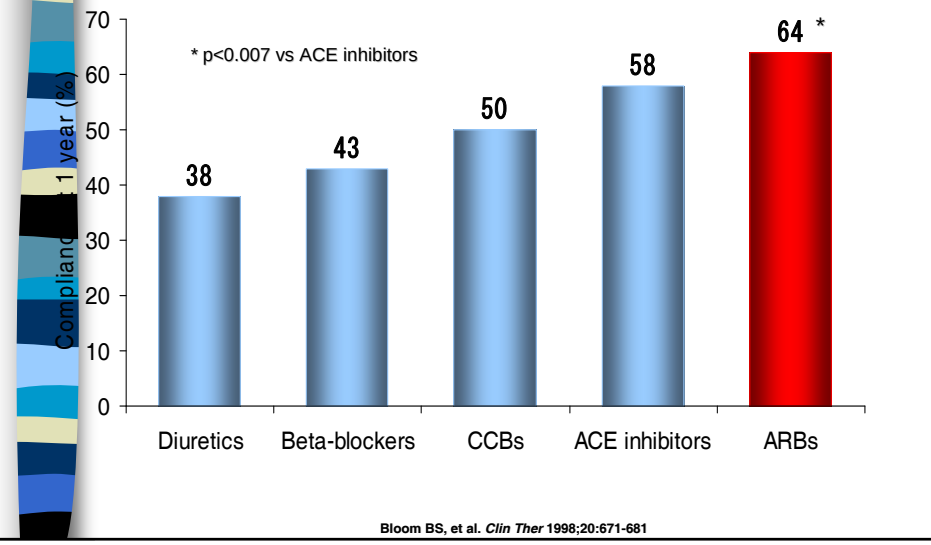


MI=myocardial infarction; HTN=hypertension; PS=psychosocial; RFs=risk factors.
Reproduced with permission from Yusuf S, et al. *Lancet* 2004;364:937-952.

History of antihypertensive drugs



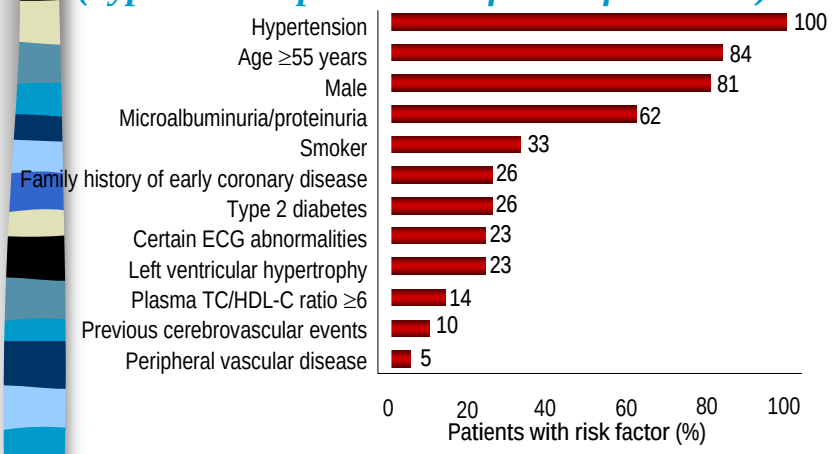
Compliance at 1 year with antihypertensive treatment



Bloom BS, et al. *Clin Ther* 1998;20:671-681

ASCOT-LLA: Patient population routinely seen in clinical practice

(hypertension plus ≥3 risk factors for CHD)*



Two of the most common additional risk factors were male sex and age ≥55 years – representative of patients frequently seen in practice

*These risk factors were used as inclusion criteria for the study.

Sever PS, et al, for the ASCOT Investigators. *Lancet* 2003;361:1149-1158

Total CV risk management key to reducing CV risk

- The demographic transition from high to low death rates (ie, the aging of the population) worldwide is predicted to increase the CV burden
- CV risk increases with age, CV risk factors often cluster and have multiplicative effects
- The evidence shows that controlling *total* CV risk decreases CV events greater than controlling a single risk factor
  - Hypertension may be a gateway to total CV risk management
- Current guidelines recognize the importance of total CV risk management

JNC 7 Compelling Indications

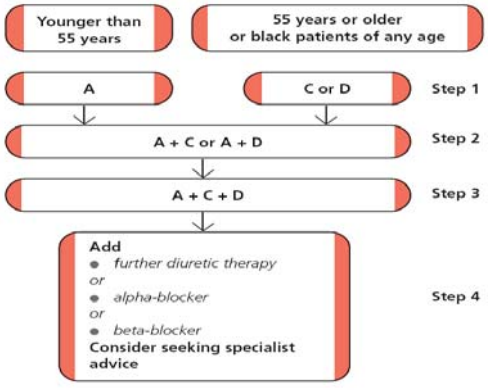
	Diuretic	BB	ACEI	ARB	CCB	AA
Heart Failure	✓	✓	✓	✓		✓
Post MI		✓	✓			✓
CAD risk	✓	✓	✓		✓	
Diabetes Mellitus	✓	✓	✓	✓	✓	
Renal disease			✓	✓		
Recurrent stroke prevention	✓		✓			

JNC 7. *JAMA*. 2003;289:2560-2572.

Choosing drugs for patients newly diagnosed with hypertension

Abbreviations:
A = ACE inhibitor (consider angiotensin-II receptor antagonist if ACE intolerant)
C = calcium-channel blocker
D = thiazide-type diuretic

Black patients are those of African or Caribbean descent, and not mixed-race, Asian or Chinese patients



BHS

NHS
National Institute for Health and Clinical Excellence

T / P ratios of ...

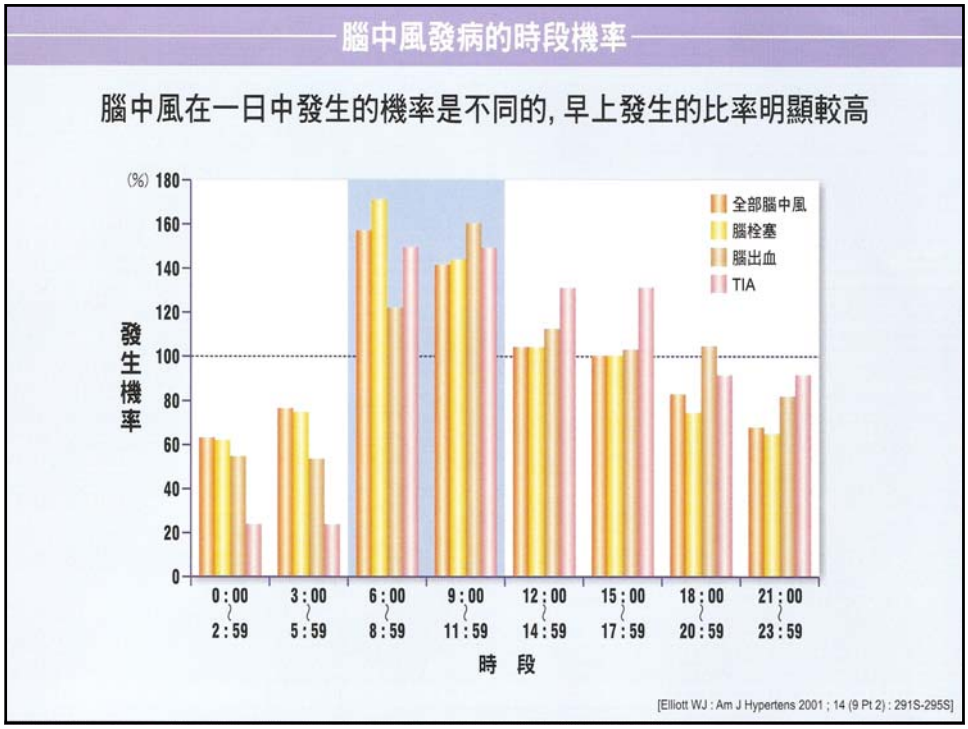
Drug	T/P Ratio	Drug	T/P Ratio
Calcium Antagonist		**ACE Inhibitor**	
Adalat OROS	0.81 - 1.07	Enalapril	0.33
Amlodipine	0.66	Lisinopril	0.25 - 0.60
Felodipine	0.47 - 0.70	Perindopril	0.33
Nicardipine	0.40		
		B-Blockers	
		Atenolol	0.40

The FDA uses the T/P ratio as a parameter for the evaluation of both the efficacy and duration of therapeutic effect for an antihypertensive drug. For a complete therapeutic coverage, the T/P ratio should be > 0.5 and to obtain maximum therapeutic benefit the antihypertensive effect should be constant without excessive variation within the 24 hour period.

Calculation of T/P Ratio:

$$\text{T/P ratio} = \frac{\downarrow \text{mmHg(Trough)} - \downarrow \text{mmHg(Placebo)}}{\downarrow \text{mmHg(Peak)} - \downarrow \text{mmHg(Placebo)}}$$

- ✶Placebo effect should be substrated.
- ✶Use of 24h ABPM
- ✶Generally, use DBP



部分高血壓表現不同形式

- 1. 失去夜間「下沉」(nocturnal dipping)，
  指血壓下降幅度<10%
- 2. 極端夜間「下沉」，指血壓下降幅度>20%。
- 3. 早晨的血壓上升「波濤」(surge) 。
- 4.一般而言，晝夜波動變化女性較顯著，老人則反之。

- 有此晨間波濤，心血管病變危險性更大。
- 失去血壓下沉和各個器官受損害的程度及左心室質量指數(心臟功能指標)有關。
- 實際操作量血壓，無症狀，一天可以量2次，也就是晨起與睡前。
- 給藥模式：

  CCB如Adalat-oros 於夜間服用，或 α-1阻斷劑在晚上；而ARA如 Diovan 在早上用，即治療時序學(chronotherapeutics)

Position statement

antihypertensive treatment: Preferred drugs 1

- Subclinical organ damage

LVH	ACEI, CA, ARB
Asymptomatic AS	CA, ACEI
Microalbuminuria	ACEI, ARB
Renal dysfunction	ACEI, ARB

- Clinical event

Previous stroke	Any BP lowering agent
Previous MI	BB, ACEI, ARB
Angina pectoris	BB, CA
Heart failure	Diuretics, BB, ACEI, ARB antialdosterone agents

Position statement
antihypertensive treatment: Preferred drugs 2

Atrial fibrillation

recurrent	ARB, ACEI
Permanent	BB, non-dihydropiridine CA
ESRD / Proteinuria	ACEI, ARB, loop diuretics
Peripheral artery D.	CA

- Condition

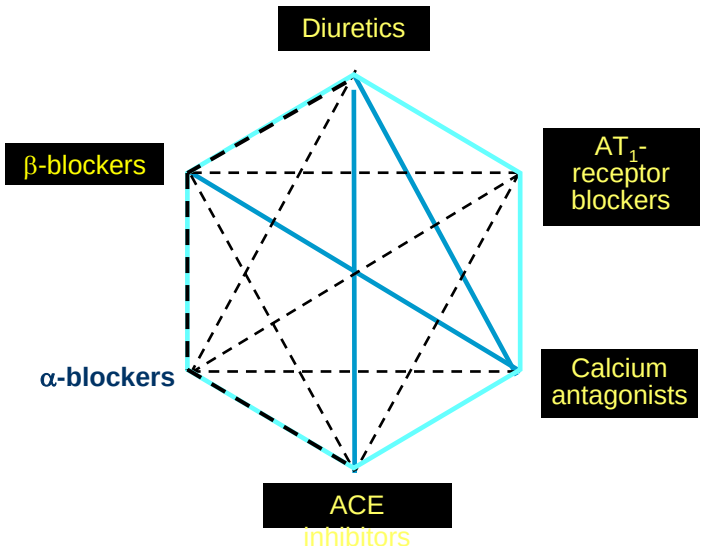
ISH (elderly)	Diuretics, CA
Metabolic syndrome	ACEI, ARB, CA
DM	ACEI, ARB
Pregnancy	CA, methyldopa, BB

First Choice(Base on clinical data & cost)

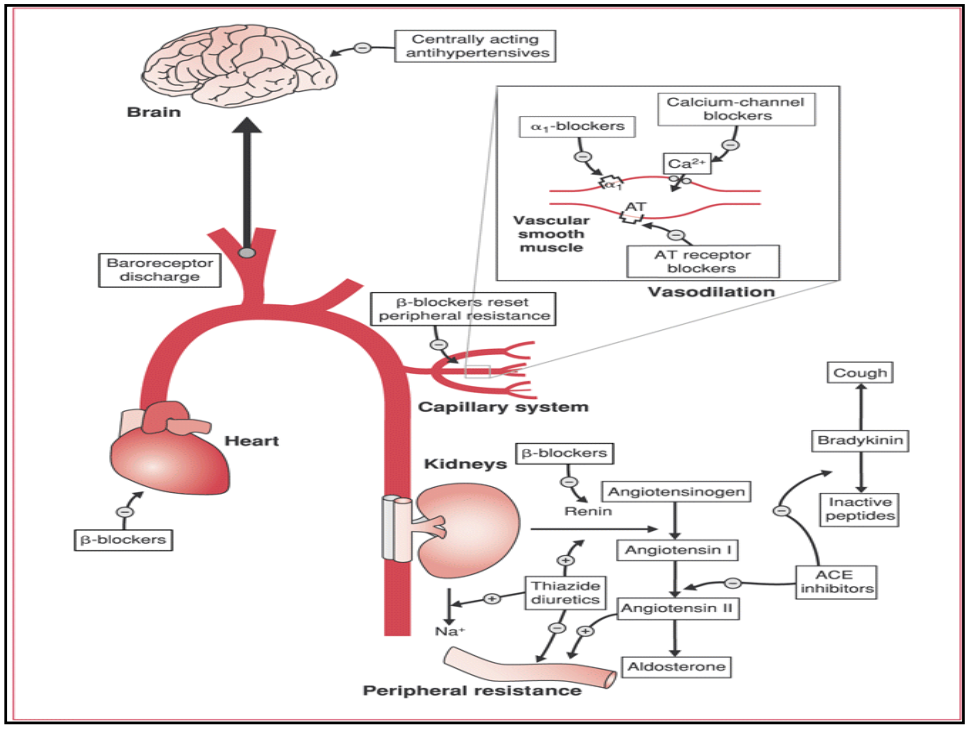
- 1. HF ACEI = ARB
- 2. Post-MI ACEI > ARB
- 3. High CV risk ACEI > ARB
- 4. Diabetes ACEI > ARB
- 5. Recurrent sroke ACEI = ARB
- 6. CKD
  - DM ACEI < ARB
  - Non-DM ACEI

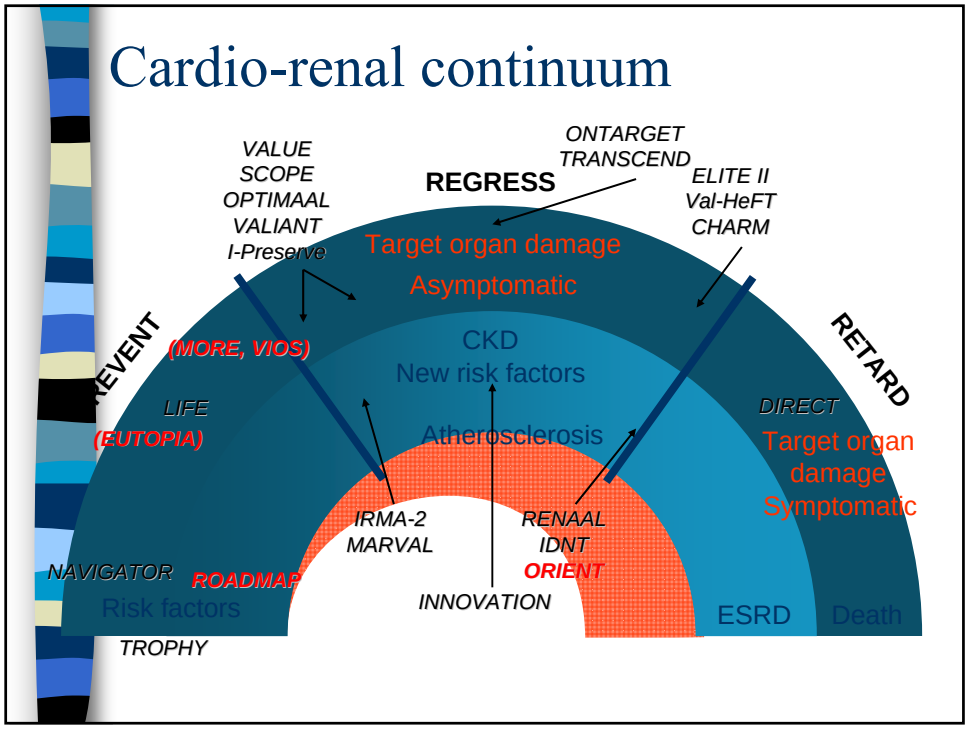
降血壓用藥分類

- diuretics
- β blocker
- α blocker
- ACEI
- Calcium Channel blocker
- Angiotensin II Receptor Antagonists
- Direct Renin inhibitor , Rasilez



Possible combinations of different classes of antihypertensive agents. The most rational combinations are represented as thick lines. ACE, angiotensin-converting enzyme. The frames indicate classes of angihypertensive agents proven to be beneficial in controlled interventional trials.


Centrally acting antihypertensives
Brain
Calcium-channel blockers
α1-blockers
Ca2+
AT
Vascular smooth muscle
AT receptor blockers
Vasodilation
Baroreceptor discharge
β-blockers reset peripheral resistance
Capillary system
Heart
Kidneys
β-blockers
Angiotensinogen
Renin
Angiotensin I
Angiotensin II
Thiazide diuretics
Na+
ACE inhibitors
Cough
Bradykinin
Inactive peptides
Aldosterone
Peripheral resistance
β-blockers

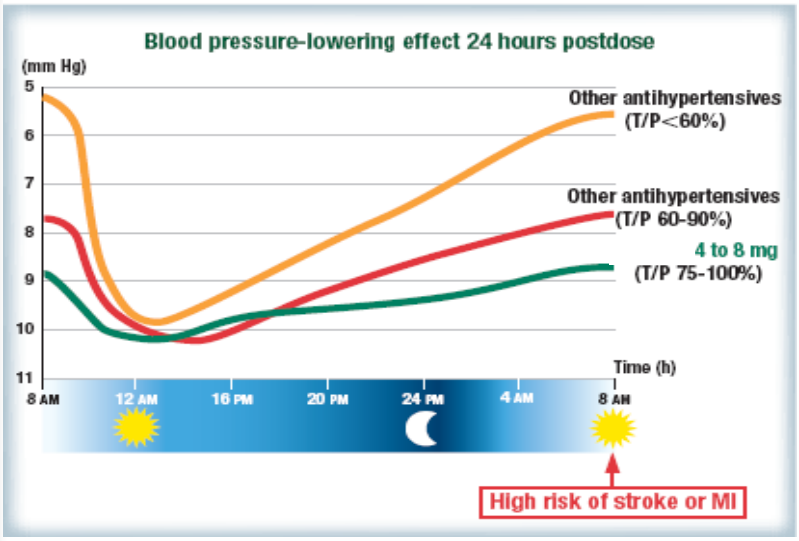

Cardio-renal continuum
VALUE
SCOPE
OPTIMAAL
VALIANT
I-Preserve
ONTARGET
TRANSCEND
REGRESS
ELITE II
Val-HeFT
CHARM
Target organ damage
Asymptomatic
(MORE, VIOS)
CKD
New risk factors
LIFE
(EUTOPIA)
Atherosclerosis
DIRECT
Target organ damage
Symptomatic
IRMA-2
MARVAL
RENAAL
IDNT
ORIENT
INNOVATION
NAVIGATOR
ROADMAP
Risk factors
TROPHY
ESRD
Death

Effective 24-hour BP Efficacy is Important

- The use of antihypertensive agents providing 24-h BP efficacy on a once-daily basis is recommended
- The advantages of such medications include improvement in adherence to therapy and minimisation of BP variability
- This may result in greater protection against the risk of major cardiovascular (CV) events and the development of target-organ damage

ESH-ESC Guidelines Committee. J Hypertens 2007;25:1105–87
Nishimura et al. Clin Exp Hypertens 2005;27:477–89

Leading to better BP control over the 24-h



Physicians' Desk Reference. 55th ed. Montvale, NJ: Medical Economics Company; 2001.
Morg Cardiol. 1995;suppl 1:57-59

糖尿病的分類

- **第1型糖尿病**(β細胞破壞，通常會造成胰島素絕對性缺乏)
  A. 自體免疫(autoimmune)
  B. 非特異性(idiopathic)
- **第2型糖尿病** (以胰島素阻抗為主，併有胰島素分泌缺乏者，或以胰島素分泌缺乏為主且併有或不併有胰島素阻抗者)
- **其他型糖尿病**
  β細胞功能之遺傳性缺陷
  胰島素功能之遺傳性缺陷
  胰臟外分泌之疾病
  內分泌疾病
  藥物或化學試劑誘發
  感染
  罕見之免疫性疾病
  其他遺傳性症候群相關之糖尿病
- **妊娠型糖尿病**

糖尿病的定義

- 糖尿病是一種**慢性高血糖的代謝疾病**，因胰島素分泌及功能異常(胰島素阻抗)，造成葡萄糖、脂肪和蛋白質的代謝異常。第1型糖尿病是因胰島素分泌缺乏，而第2型糖尿病則是胰島素的分泌及功能異常，造成血中葡萄糖濃度增高。

糖尿病大都是因為**高血糖的症狀**(例如：多尿、多喝、體重減輕、多吃)才被診斷出來，但近年來，特別注重在葡萄糖代謝異常或尚未出現症狀時，即應**早期診斷**。

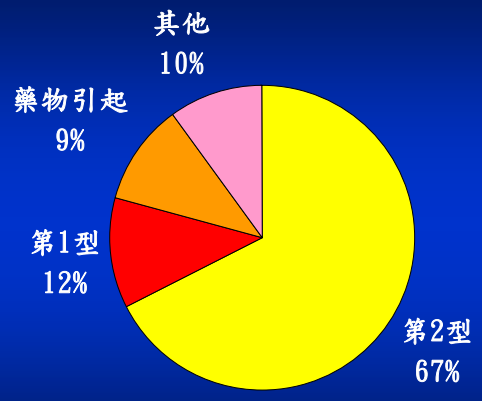
- 糖尿病長期控制不良造成**多發性器官損害**，例如：視網膜病變、腎臟病變、神經病變和自律神經功能異常。糖尿病人特別容易罹患心血管、腦血管和周邊血管疾病等。

台灣糖尿病的流行病學

- **第1型糖尿病**[1]
  - 發生率：每年每10萬人口數1.5人
- **第2型糖尿病**[2-5]
  - **盛行率：4.9% - 9.2%**
  - 危險因子：年紀大、肥胖、糖尿病家族史、高血壓、身體活動少，高三酸甘油酯血症

1 Chuang LM et al., Diabetes Res Clin Pract 50:S41-S47, 2000.
2 Tai TY et al., J Med Assoc Thai 70 (suppl 2):49-53, 1987.
3 Lin JD et al., Diabetes Res Clin Pract 20:75-85,1993.
4 Chou P et al. Diabetes Care 17:1055-1058, 1994.
5 Lu FH et al., Diabet Med 15:564-572, 1998.

台灣學童新發生的糖尿病以第2型為主



- 6-18歲學童
- 第2型糖尿病發生率:每年每10萬人口數6.5人
- 以第2型糖尿病為主，約為第1型糖尿病的5.6倍
- 第2型糖尿病的危險因子:肥胖、青春期、高血壓、高膽固醇血症以及家族史

Wei JN et al. *JAMA* 290:1345-1350, 2003

糖尿病的診斷

	靜脈血漿葡萄糖值(mg/dl)
糖尿病（Diabetes mellitus，DM）：	
空腹　且/或	≧126
葡萄糖給予後 2 小時/或隨機	≧200
葡萄糖失耐（Impaired glucose tolerance，IGT）：	
空腹（若有測）且	＜126
葡萄糖給予後 2 小時	140-199
空腹血糖偏高（Impaired fasting glucose，IFG）：	
空腹　且	100-125
葡萄糖給予後 2 小時（若有測）	＜140

區分第 1 型或第 2 型糖尿病

	第 1 型糖尿病	第 2 型糖尿病
發病	急性－有明顯症狀	慢性－通常無症狀
臨床表現	● 體重減輕 ● 多尿 ● 頻渴	● 肥胖 ● 有明顯的第 2 型糖尿病家族史 ● 種族－高盛行率的族群 ● 黑色棘皮症（Acanthosis Nigricans） ● 多發性囊泡卵巢症候群（Polycystic Ovary Syndrome）
血中酮體	常常出現	通常沒有
C-胜肽	低或無	正常或高
升糖素刺激後血清C-胜肽濃度	低（＜0.7 ng/ml）或無	正常或高
自體抗體	● ICA陽性 ● Anti-GAD_{65}陽性 ● ICA 512 陽性	● ICA 陰性 ● Anti-GAD_{65}陰性 ● ICA 512 陰性
治療	使用胰島素	改變生活型態、口服抗糖尿病藥或胰島素
自體免疫疾病的關聯性	多數有	無

無症狀成年人之糖尿病前期和糖尿病的篩檢*

1 、BMI ≧24 kg/m2且併有一個危險因子以上者**：

- 缺乏運動
- 一等親人罹患糖尿病
- 高危險族群(Asian，African American，Latino，Native American，Pacific Islanders)
- 生產超過4kg以上嬰兒或曾診斷為妊娠型糖尿病者
- 血壓≧140/90 mmHg或已服用治療高血壓藥物者
- HDL＜35 mg/dl，或三酸甘油酯≧250 mg/dl
- 多發性囊泡卵巢症候群的婦女
- IGT或IFG
- 臨床上表現顯著胰島素阻抗者(例如：病態性肥胖，黑色棘皮症)
- 心血管疾病者

2、若無上述條件，45歲以上者

3、篩檢正常者，至少每隔三年再篩檢一次

* 測量空腹血糖或做口服葡萄糖耐受試驗

** 符合1者為高風險群

對民眾糖尿病的早期篩檢方法之建議

- 高風險群民眾：測定血漿葡萄糖(空腹或口服葡萄糖耐受試驗)。
- **患有心血管疾病和妊娠型糖尿病者：強烈建議口服葡萄糖耐受試驗。**

急性心肌梗塞的病人，建議安排葡萄糖耐受試驗(Euro Heart Survey)

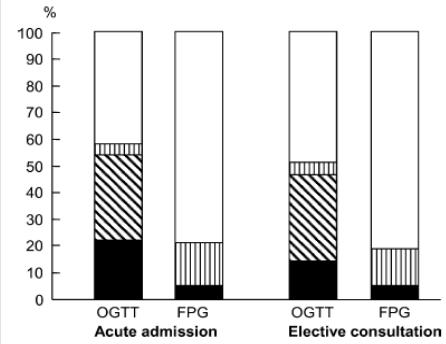
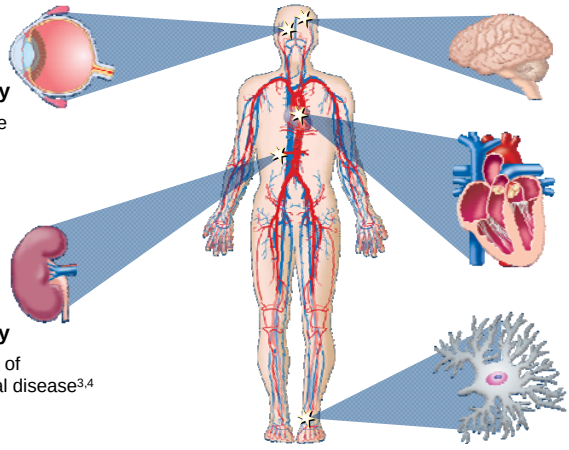


Fig. 2 Comparison of glucometabolic characterisation by means of an oral glucose tolerance test (OGTT) or fasting plasma glucose (FPG) only. Data from patients without previously known diabetes in whom an OGTT was performed giving the opportunity to either express glucometabolic state based either on the FPG represented by OGTT (0 min) or the full information from the OGTT including both OGTT (0 min) and the 2 h post-load plasma glucose OGTT (2 h) See text for further information. □ = normal; ▥ = impaired fasting glucose; ▧ = impaired glucose tolerance; ■ = newly detected diabetes.

- 本研究針對25個歐洲國家110家醫院，共4196位因冠心病住院的人進行研究
- 在923位沒有糖尿病史，因急性冠心症住院的人中，36%為葡萄糖失耐， 22%新診斷出糖尿病
- 在997位沒有糖尿病史，因stable CAD住院者， 37%為葡萄糖失耐， 14%的人新診斷出糖尿病

Bartnik M et al. Eur Heart J 2004;25:1880-1890

Diabetes is associated with serious complications



Diabetic Retinopathy

Leading cause of blindness in adults[1,2]

Diabetic Nephropathy

Leading cause of end-stage renal disease[3,4]

Stroke

2- to 4-fold increase in cardiovascular mortality and stroke[5]

Cardiovascular Disease

8/10 individuals with diabetes die from CV events[6]

Diabetic Neuropathy

Leading cause of non-traumatic lower extremity amputations[7,8]

[1]UK Prospective Diabetes Study Group. *Diabetes Res* 1990; 13:1–11. [2]Fong DS, *et al. Diabetes Care* 2003; 26 (Suppl. 1):S99–S102. [3]The Hypertension in Diabetes Study Group. *J Hypertens* 1993; 11:309–317. [4]Molitch ME, *et al. Diabetes Care* 2003; 26 (Suppl. 1):S94–S98. [5]Kannel WB, *et al. Am Heart J* 1990; 120:672–676. [6]Gray RP & Yudkin JS. Cardiovascular disease in diabetes mellitus. In *Textbook of Diabetes* 2nd Edition, 1997. Blackwell Sciences. [7]King's Fund. *Counting the cost.* The real impact of non-insulin dependent diabetes. London: British Diabetic Association, 1996. [8]Mayfield JA, *et al. Diabetes Care* 2003; 26 (Suppl. 1):S78–S79.

Treatment Guidelines: Glycemic Goals

Glycemic Profiles	IDF[1]	ADA EASD[2]	ACE AACE[3]	UK NICE[4]	Canada[5]	Taiwan CTDA[6]
A1c (%)	<6.5	<7	<6.5	<6.5-7.5[a]	<7	<6.5
FPG (mg/dL)	<110	<130	<110	<126	<126	<110
PPG (mg/dL)	<145[b]	<180[c]	<140	<153	<180[d]	<145

a: A1c<6.5% for monotherapy or two drug combination, <7.5% for ≧3 drug combination.
b: post-prandial 1-2 hours.
c: post-prandial 1.5-2 hours.
d: <144 mg/dL if A1c goal not being met

1. IDF, Global Guidelines for Type 2 Diabetes, August 2005.
2. ADA/EASD Consensus, Nathan DM, et al. Diabetologia 2009;52:17–30
3. ACE/AACE, Endocrine Practice 2007; 13 (3): 261-268
4. UK NICE, Type 2 diabetes: national clinical guideline for management in primary and secondary care. London: Royal College of Physicians, 2008.
5. Canadian Guidelines, Canadian Journal of Diabetes 2008; 32 (Suppl 1):S1-S201
6. Taiwan CTDA, 中華民國糖尿病醫學會2006第二型糖尿病治療指引

飲食計畫

- 體重控制
  - 過重者，建議 3-6 月內減少原體重 5-10%。
- 脂肪
  - 飽和脂肪少於總熱量的 10%。
  - 避免或限制肥肉、動物性脂肪、全脂奶製品、棕櫚油、椰子油、反式脂肪、加工食物等。
  - 以單元不飽和脂肪或高纖醣類食物來取代飽和脂肪。
- 碳水化合物
  - 碳水化合物與單元不飽和脂肪酸可佔總熱量 60-70%。
  - 主餐以碳水化合物為主，搭配高纖維食物，如：蔬菜、豆類、全穀類及水果。
  - 可攝取少量糖份，非營養性甜味劑亦可適量使用。
  - 每天三餐，平均分配碳水化合物。

飲食計畫

- 蛋白質
  - 不超過總熱量 20%。
  - 好的蛋白質來源：魚、海鮮、瘦肉、雞、低脂奶製品、堅果及豆類。
- 酒精
  - 飲酒每天不應超過 1-2 份量（standard drink）。
    - 所謂一個份量相當於 285 ml 的啤酒、375 ml 的淡啤酒、100 ml 的葡萄酒或 30 ml 的烈酒。一個份量相當於 12 g 純酒精的量。
  - 酒精可能會讓使用磺醯脲素或胰島素的病人引發低血糖。
- 鹽
  - 每天攝取 6 g 以下，尤其是高血壓病人。
  - 限制高鹽食物，如醃製、加工食品、醬料（醬油、蠔油、魚露），儘可能選擇新鮮的天然食物做為食材。

飲食計畫

- 可多吃
  - 這些食物當成每餐的基礎。
  - 例如：蔬菜、豆莢類、扁豆類、麵、米、全麥麵包、五穀類米、大麥、全麥穀類、新鮮水果。
  - 要注意很多加到食物中的醬料及防腐劑富含鹽份、糖或油脂，應避免食用。
- 適量吃
  - 吃少量富含蛋白質的食物。
  - 例如：魚、海鮮、蛋、瘦肉、去皮雞肉、堅果類、低脂起士、低脂優格、低脂牛奶。
- 要少吃
  - 儘量減少脂肪、糖及酒精的攝取。
  - 例如：油、奶油、動物性脂肪、氫化奶油、椰奶、椰奶油、加工肉品、油炸的食物、含有防腐劑或加工的食物、酥皮點心、甜點、餅乾、軟性飲料（soft drink）。

增加體能活動

- 是治療第 2 型糖尿病的重要方法
  - 可增加胰島素敏感度、改善血糖控制以及幫助減輕體重等。
  - 規律運動，明顯降低糖尿病人在 12-14 年中之死亡率。
- 一般的目標
  - 中等強度體能活動：包括健走、打太極拳、騎單車、打高爾夫球及園藝等，每週至少 150 分鐘。
  - 持久的中度或更強之體能活動（如跳舞、有氧運動、慢跑、持續來回游泳、單車爬坡、園藝之挖鏟等）可獲得更多的益處。
  - 肌力活動（如重力訓練）：每週至少 2 次。針對小腿、大腿、手臂、肩膀、軀幹的主要肌肉群，強調使用輕度到中度阻力，每部位重複 8-12 下。
  - 依照年齡、社會、經濟、文化及體能狀態選擇適合個人之體能活動計畫。

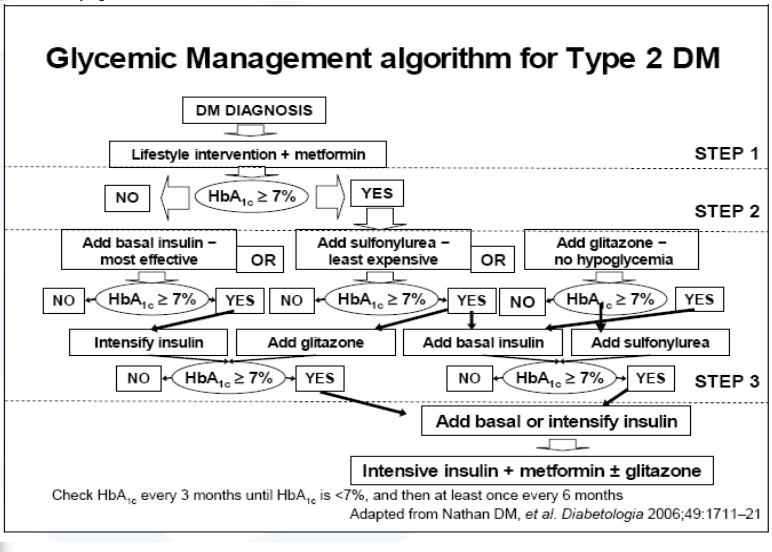
增加體能活動

- 應避免做
  - 長時間坐著不動，例如：看電視、上網、打電玩。
- 應規律做
  - 積極參與休閒活動及娛樂性的運動，例如：快走、高爾夫球、耐力訓練、騎單車及球類運動。
  - 333 運動標準。
    - 每週運動 3 次、每次 30 分鐘、每次心跳 130 次/分以上。
    - HRmax = 220 – 病人年齡
    - 下限 = 0.5（ HRmax – HRrest ）+ HRrest
    - 上限 = 0.74（ HRmax – HRrest ）+ HRrest
- 應天天做
  - 養成健康生活習慣，例如：走路到商店購物、走樓梯少搭電梯、少打電話用走的到同事辦公室當面討論聯繫、溜狗等。
  - 健走運動:每日一萬步。
- 活動時應注意潛在危險，如割傷、擦傷、脫水，須特別注意足部保護。
- 額外增加或劇烈的體能活動，糖尿病人宜調整食物攝取或藥物，以免低血糖。

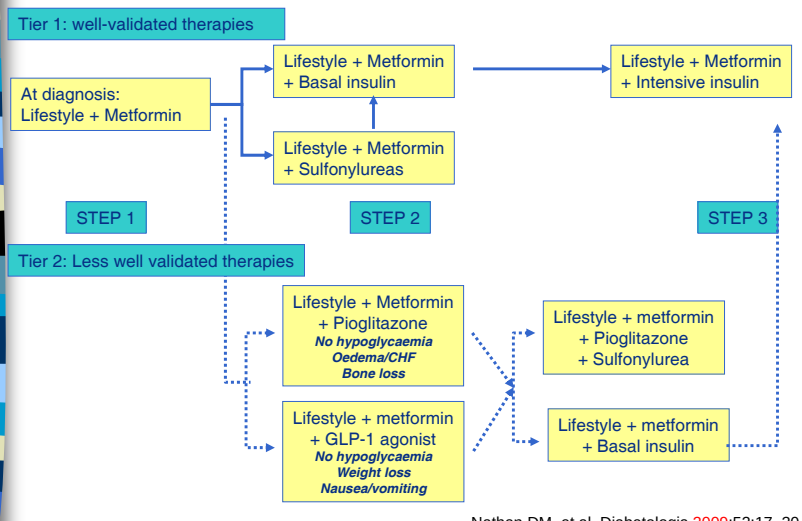
Therapy for type 1 diabetes

- use of multiple dose insulin injections (3–4 injections per day of basal and prandial insulin) or CSII therapy
- matching of prandial insulin to carbohydrate intake, premeal blood glucose, and anticipated activity
- For many patients (especially if hypoglycemia is a problem), use of insulin analogs.

Glycemic management algorith
Type 2 DM

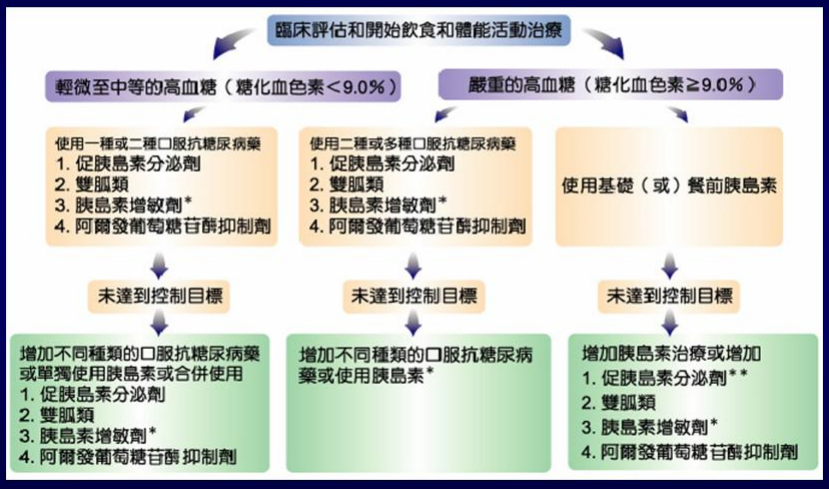


New ADA/EASD algorithm for T2DM



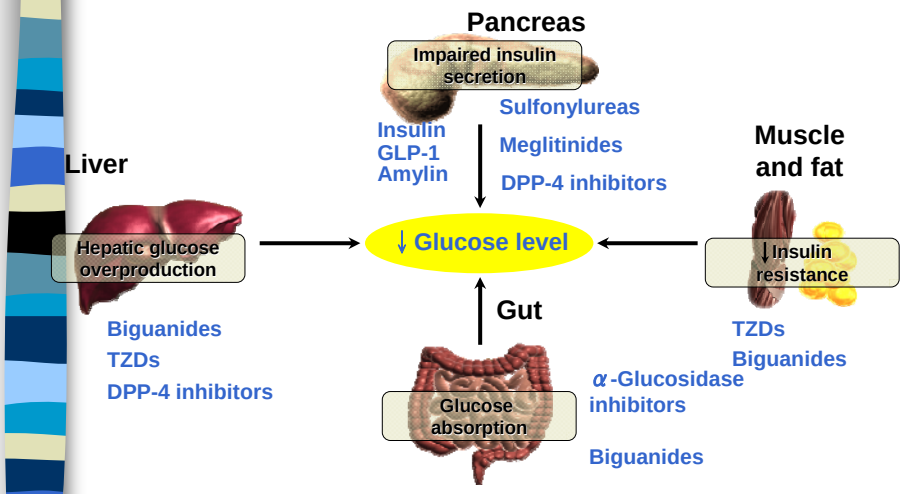
Nathan DM, et al. Diabetologia 2009;52:17–30

第 2 型糖尿病人高血糖的處理



2006/8/31 中華民國糖尿病學會 23

各類抗糖尿病藥物作用機轉



DeFronzo RA. Ann Intern Med 131:281–303,1999. Inzucchi SE. JAMA 287:360-372,2002. Porte D, et al. Clin Invest Med 18:247–254,1995.

選擇抗糖尿病藥物的建議

主要代謝異常	建議抗糖尿病藥物
餐後高血糖	α-glucosidase抑制劑、短效sulfonylurea、glinide 、短效型胰島素或速效型insulin類似物、amylin類似物、 GLP-1類似物、 DPP-4抑制劑
空腹高血糖	metformin、長效sulfonylurea、TZD、長效型胰島素或insulin類似物、GLP-1類似物、 DPP-4抑制劑
胰島素阻抗	metformin、TZD、α-glucosidase抑制劑
胰島素分泌不足	sulfonylurea、glinide、胰島素、GLP-1類似物、DPP-4抑制劑

參考2007年ESC/EASD guideline

藥物平均降低HbA1c的效力

抗糖尿病藥物	糖化血色素下降的平均值 (HbA1c,%)
α-glucosidase 抑制劑	0.5-1.0
Metformin	1.0-2.0
Glinide 類	0.5-1.5
TZD	0.5-1.5
胰島素	1.0-3.5
Sulfonylurea	1.0-2.0
GLP-1 類似物	0.5-1.0
Amylin 類似物	0.5-1.0
DPP-4 抑制劑	0.5-0.9

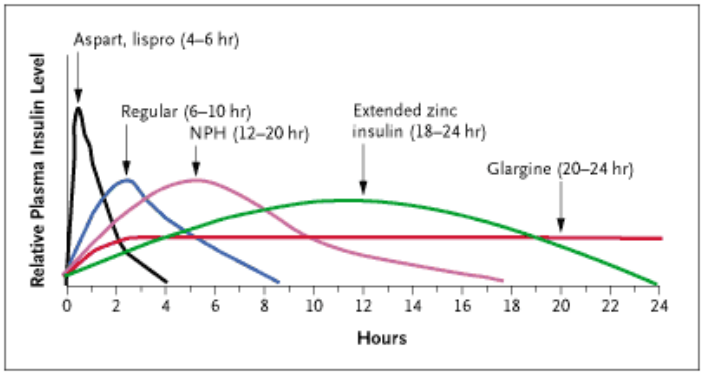
使用藥物所應注意的議題

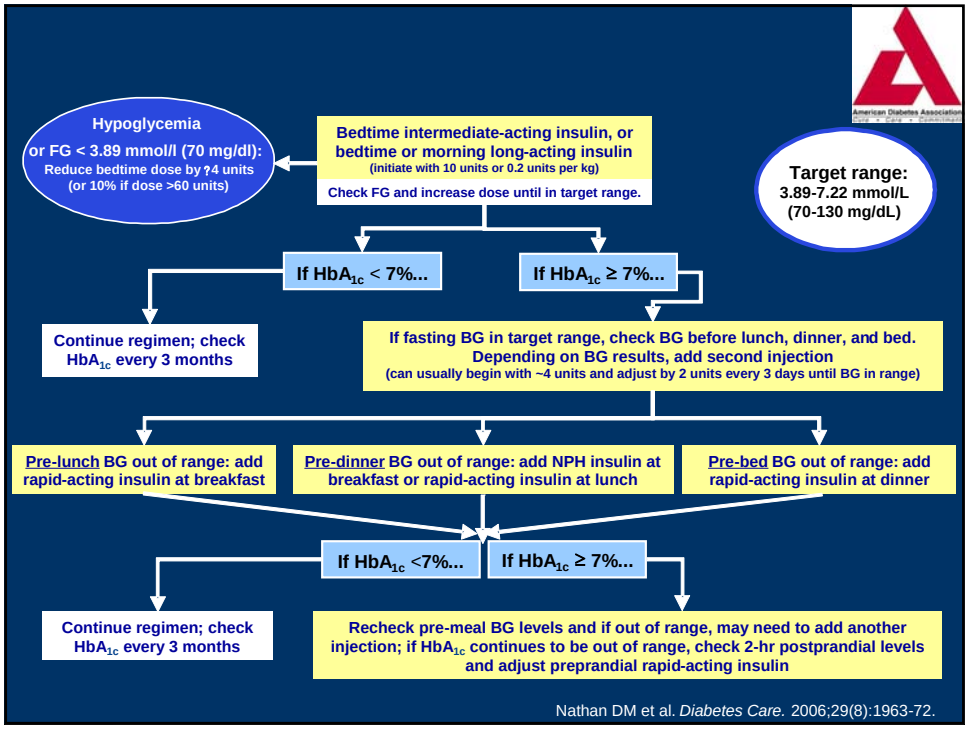
議題	需要謹慎使用的藥物
體重增加	sulfonylurea、glinide、TZD、胰島素
腸胃系統的症狀	Metformin、α-glucosidase 抑制劑、GLP-1 類似物、amylin 類似物、 DPP-4 抑制劑
低血糖	sulfonylurea、glinide、胰島素、GLP-1類似物、 amylin 類似物、DPP-4 抑制劑
腎臟功能障礙	metformin *、sulfonylurea
肝臟功能障礙	glinide、TZD、metformin、α-glucosidase 抑制劑
心肺功能障礙	metformin、TZD

*中華民國衛生署規定：男性cre≧1.5，女性cre ≧ 1.4者禁用

參考2007年ESC/EASD guideline

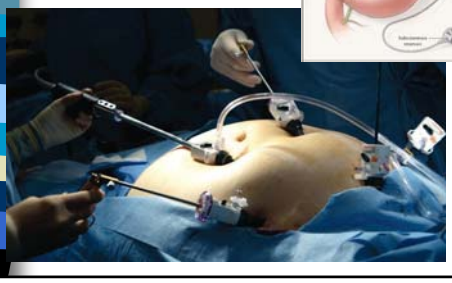
Insulins and Insulin Analogues

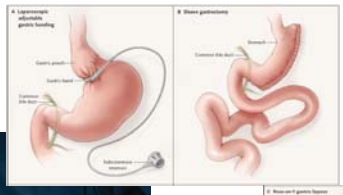


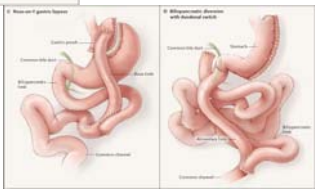


Bariatric surgery

- Bariatric surgery should be considered for adults with BMI ≧35 kg/m2 and type 2 diabetes, especially if the diabetes is difficult to control with lifestyle and pharmacologic therapy.







Bariatric surgery for morbid obesity

- Diabetes was completely resolved in 76.8% of patients and resolved or improved in 86.0%.
- Hyperlipidemia improved in 70% or more of patients.
- Hypertension was resolved in 61.7% of patients and resolved or improved in 78.5%.
- Obstructive sleep apnea was resolved in 85.7% of patients and was resolved or improved in 83.6% of patients.

Buchwald H. et al *JAMA 2005;293:1724-37*

低血糖的處置

- 意識清楚的患者
  - 給予口服碳水化合物，例如：方糖、葡萄糖。
- 意識不清的患者
  - 給予靜脈注射 20 ml 50% 葡萄糖或肌肉注射 0.5-1 mg 的升糖素（glucagon）。病人意識恢復後，應立即給予口服碳水化合物。
- 若低血糖是因長效磺醯脲素（或長效型胰島素）所造成，低血糖的時間可能會延長，應持續監測血糖至少 24-48 小時，可能須長時間靜脈輸注葡萄糖，並住院觀察。

Blood pressure control

- Blood pressure should be measured at every routine diabetes visit.
- Patients with diabetes should be treated to a systolic blood pressure $<$130 mmHg and diastolic blood pressure $<$80 mmHg.
- Pharmacologic therapy for patients with diabetes and hypertension should be with a regimen that includes either an ACE inhibitor or an angiotensin receptor blocker (ARB).

Lipid control

- In most adult patients, measure fasting lipid profile at least annually.
- In individuals without overt CVD, the primary goal is an LDL cholesterol $<$100 mg/dl.
- Triglycerides levels $<$150 mg/dl and HDL cholesterol $>$40 mg/dl in men and $>$50 mg/dl in women are desirable.
- LDL cholesterol–targeted statin therapy remains the preferred strategy.

Aspirin therapy

- Use aspirin therapy (75–162 mg/day) as a primary prevention strategy in those with type 1 or type 2 diabetes at increased cardiovascular risk, including those who are 40 years of age or who have additional risk factors (family history of CVD, hypertension, smoking, dyslipidemia, or albuminuria). (C)
- Use aspirin therapy (75–162 mg/day) as a secondary prevention strategy in those with diabetes with a history of CVD. (A)

抗血小板藥物－臨床建議

臨床建議	證據等級	臨床建議強度	華人資料
針對第2型糖尿病且超過40歲，或合併其他心血管疾病危險因子的病人(包括心血管疾病家族史、高血壓、吸菸、高脂血症或(微量)白蛋白尿等)，建議使用低劑量的aspirin（每天75-162 mg)，以預防心血管疾病(初級預防)	中	中等建議	無
針對第2型糖尿病且合併有心血管疾病史的人(包括心肌梗塞、血管繞道手術、腦中風或暫時性腦缺血、周邊血管疾病、間歇性跛行、心絞痛等)，建議使用低劑量的aspirin (每天75-162 mg)，以預防心血管疾病(次級預防)	高	強烈建議	無
針對第1型糖尿病且超過40歲，或合併其他心血管疾病危險因子的病人(包括心血管疾病家族史、高血壓、吸菸、高脂血症或(微量)白蛋白尿等)，建議使用低劑量的aspirin(每天75-162 mg/day)，以預防心血管疾病(初級預防)	低	中等建議	無

糖尿病人常規檢查項目

	最低的篩檢頻率	篩檢步驟
眼睛	2 年	● 散瞳的眼底檢查 ● 視力
腎臟	1 年	● 尿液白蛋白測量
足部	1 年	● 臨床神經學及血管評估 ● 檢視足部及鞋子
血壓	每次門診	● 休息 5 分鐘後，坐著測量
血脂	1 年	● 血中脂肪的濃度
血糖控制	6 個月	● 糖化血色素

其他控制目標及介入標準

參數	目標
糖化血色素	<6.5%
血壓	<130/80 mmHg
總膽固醇	<174 mg/dl
低密度脂蛋白膽固醇	<100 mg/dl
高密度脂蛋白膽固醇	>40 mg/dl
三酸甘油酯	<150 mg/dl
尿液白蛋白:肌酸酐比值	<30 mg/g
運動	每週至少 150 分鐘

臨床監測一覽表

測試項目	初診	追蹤	每季	每年
眼睛：視力、眼底鏡	要			要
足：脈搏、神經病變	要		要	要
體重	要	要	要	要
身體質量指數	要			要
血壓	要	要	要	要
血糖	要	要	要	要
糖化血色素	要		要	要
膽固醇/高密度脂蛋白膽固醇	要		△	要
低密度脂蛋白膽固醇	要		△	要
三酸甘油酯	要		△	要
蛋白尿*	要		△	要
肌酸酐/尿素氮	要		△	要
心電圖	要			要
尿液鏡檢	要			要

*如果設備允許且蛋白尿呈「陰性」反應，則應加測微量白蛋白尿，△：初診有異常，則需執行。

- **gestational diabetes mellitus (GDM)**

Diabetes Care *January 2004 (27):S88~S90*

Diabetes Care *July 2007 (30):S251~S260*

Definition

- Gestational diabetes mellitus (GDM) is defined as any degree of glucose intolerance with onset or first recognition during pregnancy.
- The prevalence may range from 1 to 14% of all pregnancies, depending on the population studied and the diagnostic tests employed.

Screening and diagnosis

Table 5—*Screening for and diagnosis of GDM*

Carry out GDM risk assessment at the first prenatal visit.

Women at very high risk for GDM should be screened for diabetes as soon as possible after the confirmation of pregnancy. Criteria for very high risk are:

- severe obesity
- prior history of GDM or delivery of large-for-gestational-age infant
- presence of glycosuria
- diagnosis of PCOS
- strong family history of type 2 diabetes

Screening/diagnosis at this stage of pregnancy should use standard diagnostic testing (Table 2).

All women of greater than low risk of GDM, including those above not found to have diabetes early in pregnancy, should undergo GDM testing at 24–28 weeks of gestation.

Low risk status, which does not require GDM screening, is defined as women with ALL of the following characteristics:

- age <25 years
- weight normal before pregnancy
- member of an ethnic group with a low prevalence of diabetes
- no known diabetes in first-degree relatives
- no history of abnormal glucose tolerance
- no history of poor obstetrical outcome

Screening and diagnosis

Two approaches may be followed for GDM screening at 24–28 weeks:

1. Two-step approach:
   A. Perform initial screening by measuring plasma or serum glucose 1 h after a 50-g oral glucose load. A glucose threshold after 50-g load of ≥140 mg/dl identifies ~80% of women with GDM, while the sensitivity is further increased to ~90% by a threshold of ≥130 mg/dl.
   B. Perform a diagnostic 100-g OGTT on a separate day in women who exceed the chosen threshold on 50-g screening.
2. One-step approach (may be preferred in clinics with high prevalence of GDM): Perform a diagnostic 100-g OGTT in all women to be tested at 24–28 weeks.

The 100-g OGTT should be performed in the morning after an overnight fast of at least 8 h.

To make a diagnosis of GDM, at least two of the following plasma glucose values must be found:

Fasting: ≥95 mg/dl
1 h: ≥180 mg/dl
2 h: ≥155 mg/dl
3 h: ≥140 mg/dl

Obstetric and perinatal considerations

- The presence of fasting hyperglycemia (105 mg/dl) may be associated with an increase in the risk of intrauterine fetal death during the last 4–8 weeks of gestation.
- GDM of any severity increases the risk of fetal macrosomia.
- Neonatal hypoglycemia, jaundice, polycythemia, and hypocalcemia may complicate GDM as well.
- GDM is associated with an increased frequency of maternal hypertensive disorders and the need for cesarean delivery.

Obstetric and perinatal considerations

- Women with GDM are at increased risk for the development of diabetes, usually type 2, after pregnancy.
- Obesity and other factors that promote insulin resistance appear to enhance the risk of type 2 diabetes after GDM, while markers of islet cell–directed autoimmunity are associated with an increase in the risk of type 1 diabetes.
- Offspring of women with GDM are at increased risk of obesity, glucose intolerance, and diabetes in late adolescence and young adulthood.

Monitoring

- Daily self-monitoring of blood glucose (SMBG)
- Urine ketone monitoring
- Blood pressure and urine protein monitoring
- Increased surveillance for pregnancies at risk for fetal demise
- Assessment for asymmetric fetal growth by ultrasonography

Management

- nutritional counseling
- adequate calories and nutrients to meet the needs of pregnancy
- Restriction of carbohydrates to 35–40% of calories has been shown to decrease maternal glucose levels and improve maternal and fetal outcomes

Glycemic control: GDM

- Regarding goals for glycemic control for women with GDM, recommendations from the Fifth International Workshop- Conference on Gestational Diabetes Mellitus were to target the following maternal capillary glucose concentrations:
- preprandial: ≦95 mg/dl (5.3 mmol/l) and either
  - 1-h postmeal: ≦140 mg/dl (7.8 mmol/l) or
  - 2-h postmeal: ≦120 mg/dl (6.7 mmol/l)

Management

- insulin therapy is recommended when MNT fails to maintain self-monitored glucose at the target levels
- Human insulin should be used when insulin is prescribed, and SMBG should guide the doses and timing of the insulin regimen. The use of insulin analogs has not been adequately tested in GDM.
- Oral glucose-lowering agents have generally not been recommended during pregnancy.

Diabetes Care *January 2004 (27):S88~S90*

Insulin analogues

- Of the three rapid-acting insulin analogs, lispro and aspart have been investigated in pregnancy, demonstrating clinical effectiveness, minimal transfer across the placenta, and no evidence of teratogenesis.

- Randomized controlled trials have not been carried out using long-acting insulin analogs of any type in diabetic pregnant women (insulin glargine, insulin detemir). Thus, human NPH insulin as part of a multiple injection regimen should be used for intermediate acting insulin effect in GDM.

Diabetes Care *July 2007 (30):S251~S260*

Table 1. Summary of evidence supporting complementary and alternative medicine therapies for type 2 diabetes mellitus

INTERVENTION	BODY OF EVIDENCE
Cinnamon	FBG level reduction in 2 of 3 trials
Chromium	HbA_{1c} and FBG level reduction in meta-analysis
Vanadium	FBG level reduction in uncontrolled trials
Fibre	HbA_{1c} level reduction (non-significant) in 1 of 3 trials FBG level reduction in 6 of 12 trials
Green tea	FBG level reduction in 1 of 3 trials Other benefits
Bitter melon	No benefit to HbA_{1c} or FBG levels in 2 small trials
Fenugreek	FBG level reduction in 1 of 3 trials Other benefits
Gymnema	HbA_{1c} level reduction in 2 small trials

HbA_{1c}—glycosylated hemoglobin A_{1c}, FBG—fasting blood glucose.

DPPV-I

Background and Data Summary:
FDA has completed a review of 88 cases of acute pancreatitis in patients using sitagliptin or sitagliptin/metformin. The cases were reported to FDA' s Adverse Event Reporting System (AERS) between October 2006 and February 2009. Hospitalization was reported in 58/88 (66%) of the patients, 4 of whom were admitted to the intensive care unit (ICU). Two cases of hemorrhagic or necrotizing pancreatitis were identified in the review and both required an extended stay in the hospital with medical management in the ICU. The most common adverse events reported in the 88 cases were abdominal pain, nausea and vomiting.

Lipid

- LDL-C
- HDL-C
- TG

ATP III: Lipid-Lowering Treatment Guidelines

Risk category	LDL-C goal	LDL-C level at which to initiate therapeutic lifestyle changes	LDL-C level at which to consider therapy
CHD or CHD risk equivalents (10-year risk >20%)	<100 mg/dL* (<2.6 mmol/L)	≥100 mg/dL (≥2.6 mmol/L)	≥130 mg/dL (≥3.4 mmol/L) (100-129 mg/dL [2.6-3.4 mmol/L]: drug optional)
2+ risk factors (10-year risk ≤20%)	<130 mg/dL (<3.4 mmol/L)	≥130 mg/dL (≥3.4 mmol/L)	10-year risk 10%-20%: ≥130 mg/dL(≥3.4 mmol/L) 10-year risk <10%: ≥160 mg/dL (≥4.1 mmol/L)
0-1 risk factor	<160 mg/dL (<4.1 mmol/L)	≥160 mg/dL (≥4.1 mmol/L)	≥190 mg/dL (160-190 mg/dL [4.1-4.9 mmol/L]: drug optional)

*Optional LDL-C goal of <70 mg/dL (<1.8 mmol/L) in very high-risk patients introduced in 2004
(Grundy SM, et al. *Circulation*. 2004;110:227-39)

Risk factors: FHx, HTN, smoking, male ⩾45, female ⩾55, HDL-C <40 mg/dL

Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. *JAMA*. 2001;285:2486-97

ADA Guideline 2009

Treatment recommendations and goals

- Lifestyle modification focusing on the reduction of saturated fat, trans fat, and cholesterol intake; weight loss (if indicated); and increased physical activity should be recommended to improve the lipid profile in patients with diabetes. (A)
- Statin therapy should be added to lifestyle therapy, regardless of baseline lipid levels, for diabetic patients:
  - with overt CVD (A)
  - without CVD who are over the age of 40 and have one or more other CVD risk factors. (A)

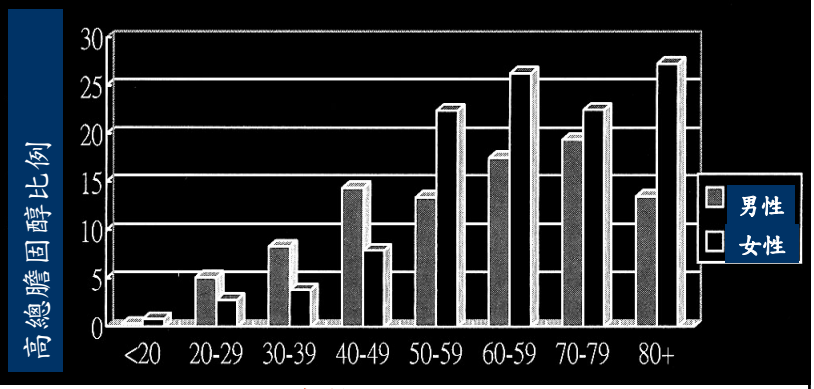
ADA Guideline 2009

Treatment recommendations and goals

- For lower-risk patients than the above (e.g., without overt CVD and under the age of 40), statin therapy should be considered in addition to lifestyle therapy if LDL-C remains above 100 mg/dl or in those with multiple CVD risk factors. (E)
- In individuals without overt CVD, the primary goal is an LDL cholesterol <100 mg/dl (2.6 mmol/l). (A)
- In individuals with overt CVD, a lower LDL cholesterol goal of <70 mg/dl (1.8 mmol/l), using a high dose of a statin, is an option. (B)

台灣地區高總膽固醇盛行率

圖 5-9 15 歲以上國人之高總膽固醇盛行率年齡分佈



資料來源: 台灣地區高血壓、高血糖、高血脂之盛行率調查

定義:總膽固醇>240或用藥

Dyslipidemia treatment

- **Pre-statin era**
- **Statin era**
  - **vs placebo** — **focus on LDL/CHD**
  - **vs statin** — **other markers/diseases**
  - **combined with non-statin**
- **New drugs**

Impact of Existing Drug Therapies on Lipid Parameters

Drug class/agents	HDL-C effect	LDL-C effect	Triglyceride effect
Bile acid sequestrants[1]	↑ 3–5%	↓ 15–30%	No change or increase
Ezetimibe*[2]	↑ 1%	↓ 18%	↓ 8%
Fibric acids[1]	↑ 10–20%	↓ 5–20%	↓ 20–50%
Nicotinic acid[1]	↑ 15–35%	↓ 5–25%	↓ 20–50%
Probucol[3]	Up to 40%	↓ 10–17%	No change
Statins[1]	↑ 5–15%	↓ 18–55%	↓ 7–30%

*Selective inhibitor of intestinal cholesterol absorption

Adapted from **1.** Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. *JAMA.* 2001;285:2486–2497. **2.** Ezetrol (ezetimibe) product information. WPC 072005. Merck Sharp and Dohme. NSW, Australia. 2006. **3.** Nippon Rinsho. 1994 Dec;52(12):3279-84.

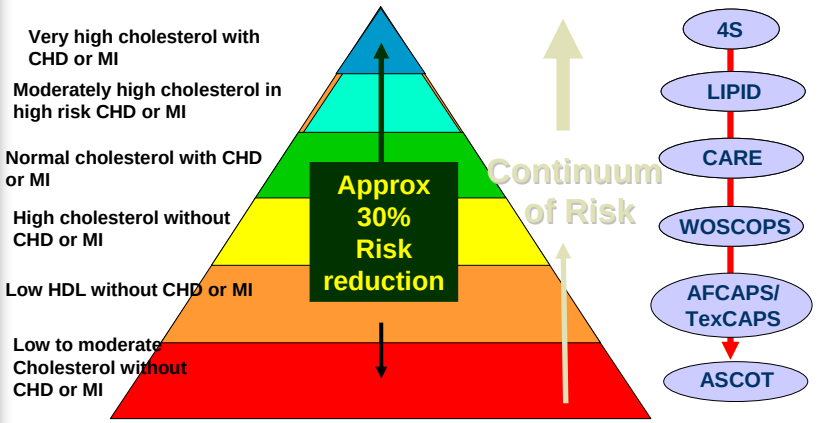
Relationship Between Changes in LDL-C and HDL-C Levels and CHD Risk

1% decrease in LDL-C reduces CHD risk by 1%[1]

1% change in HDL-C associated with 1-3% reduction in CHD risk[2-5]

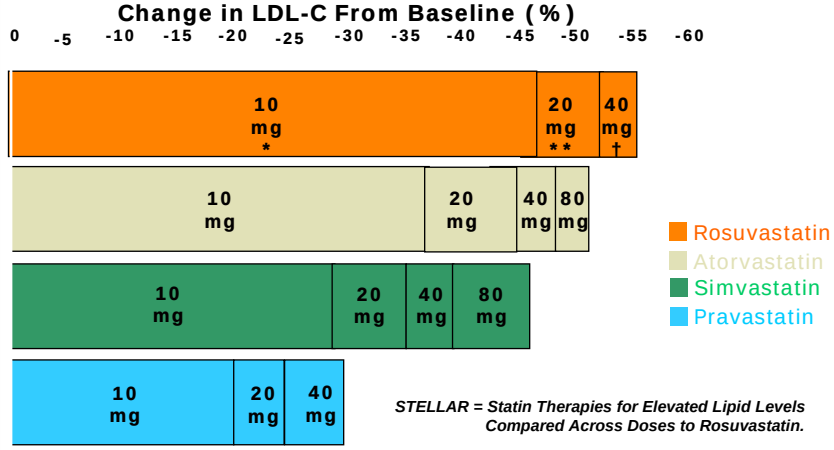
1.Grundy SM *et al*. *Circulation*. 2004; **110**: 227–39.
2.Gordon DJ, Probstfield JL, Garrison JD *et al*. *Circulation* 1989; **79**: 8-15.
3.Boden W. *American Journal of Cardiology* 2000; **86** (suppl): 19L-22L.
4.Manninen V, Elo O, Frick MH *et al*. *JAMA* 1988; **260**:641-651.
5.Rubins HB, Robins S, Collins D *et al*. *N Engl J Med* 1999; **341**:410-418

The Pyramid of Recent Trials: Relative Size of the Various Segments of the Population



Double dose of statins results in ~6% reduction of LDL

The STELLAR Trial

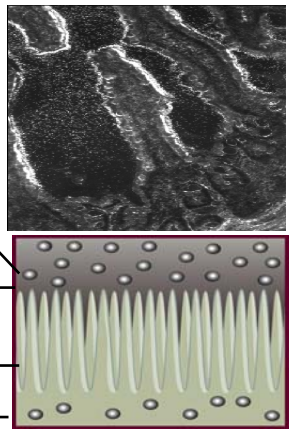


STELLAR = Statin Therapies for Elevated Lipid Levels Compared Across Doses to Rosuvastatin.

**P*<.002 vs atorvastatin 10 mg; simvastatin 10, 20, 40 mg; pravastatin 10, 20, 40 mg.
***P*<.002 vs atorvastatin 20, 40 mg; simvastatin 20, 40, 80 mg; pravastatin 20, 40 mg.
†*P*<.002 vs atorvastatin 40 mg; simvastatin 40, 80 mg; pravastatin 40 mg.
Adapted from Jones et al. *Am J Cardiol* 2003;92:152–160.

Ezetimibe: Mechanism of Action

Radiolabeled ezetimibe localized at brush border of small intestine



Photograph courtesy of Harry R. Davis, PhD.

Cholesterol is transported from the intestinal lumen, to be processed inside the enterocyte.

- Ezetimibe localizes and appears to act at the brush border of the small intestine and inhibits the absorption of cholesterol.
- This results in:
  - Decrease in delivery of intestinal cholesterol to the liver.
  - Reduction in hepatic cholesterol stores and increase in clearance of cholesterol from the blood.
- Ezetimibe inhibited 54% of all intestinal cholesterol absorption.

Summary

- LLD is associated with lower cancer mortality
- LDL-C level is still the most important parameter in lipid management
- Systolic heart failure is not an appropriate target for LDL-lowering therapy, but AF may be prevented
- Use statin before vascular surgery
- Check hs-CRP and consider statin Tx
- Lack of CV benefit with statins in both AURORA and 4D suggests that CVD in hemodialysis patients is different compared with that in a non-renal population
- Ezetimibe unlikely causes cancer

謝謝聆聽