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Type 2 DM in East Asians: Similarities and Differences

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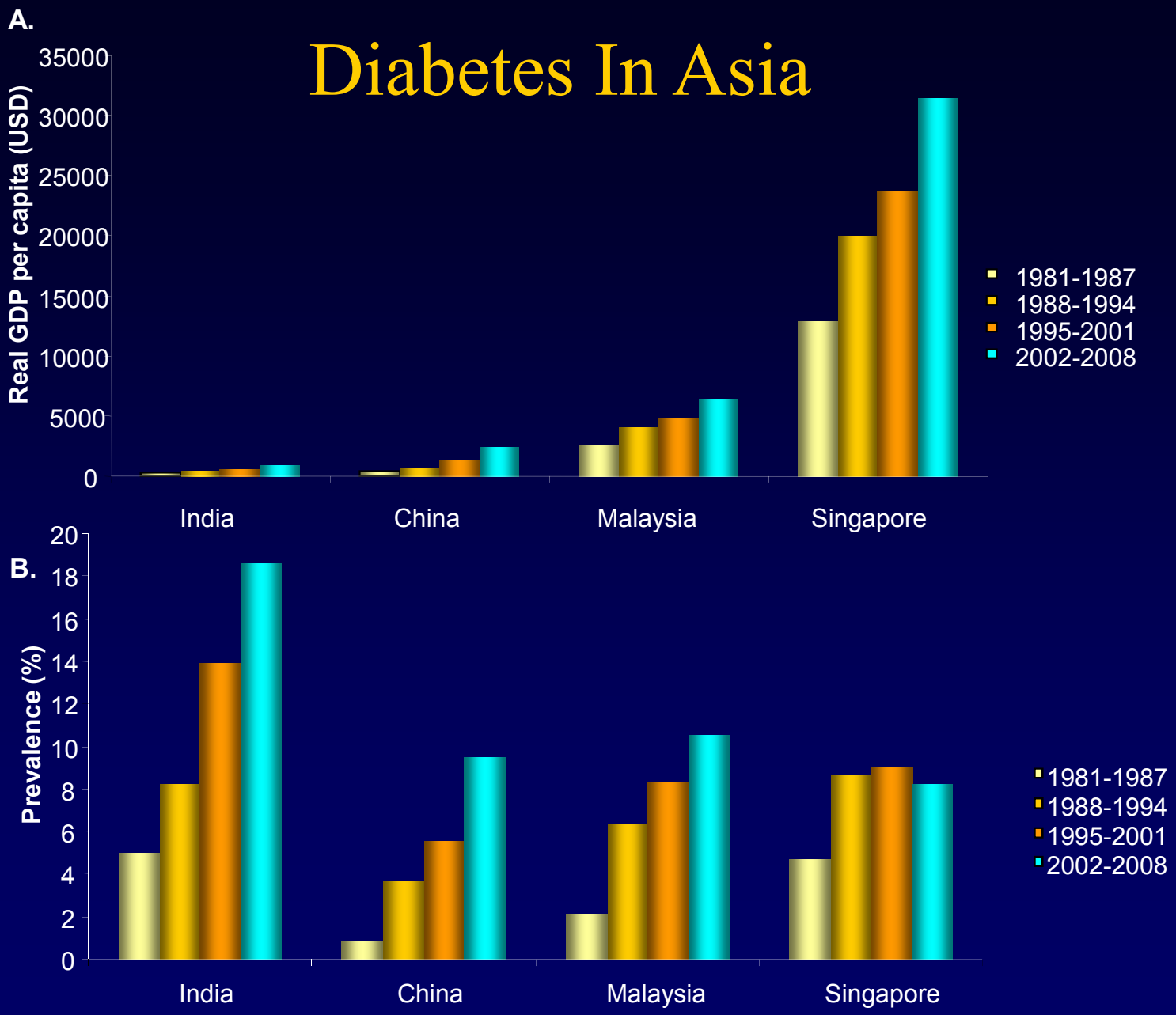
2011 - 2015

Outline

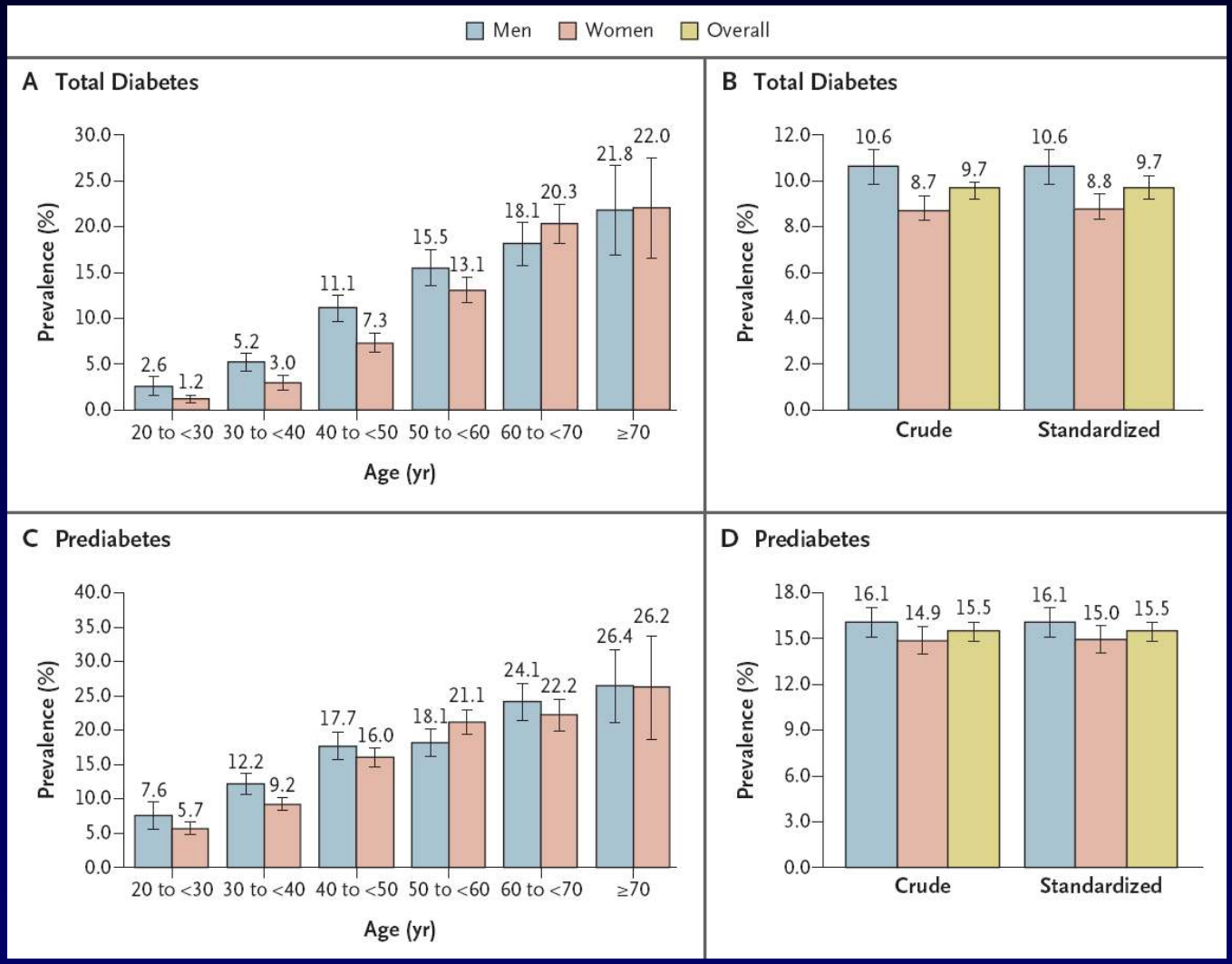
- Epidemiology of Diabetes in Asia
- Familial young-onset DM
- Genetic predictors of T2DM in E. Asians
- Pathophysiology and role of beta-cell dysfunction
- Pattern of DM complications
- Impact of gestational diabetes
- Implications for treatment and prevention

Diabetes In Asia



Ramachandran A, Ma RC and Snehalatha DC, Lancet 2010; 375: Jan 30

Prevalence of DM in China



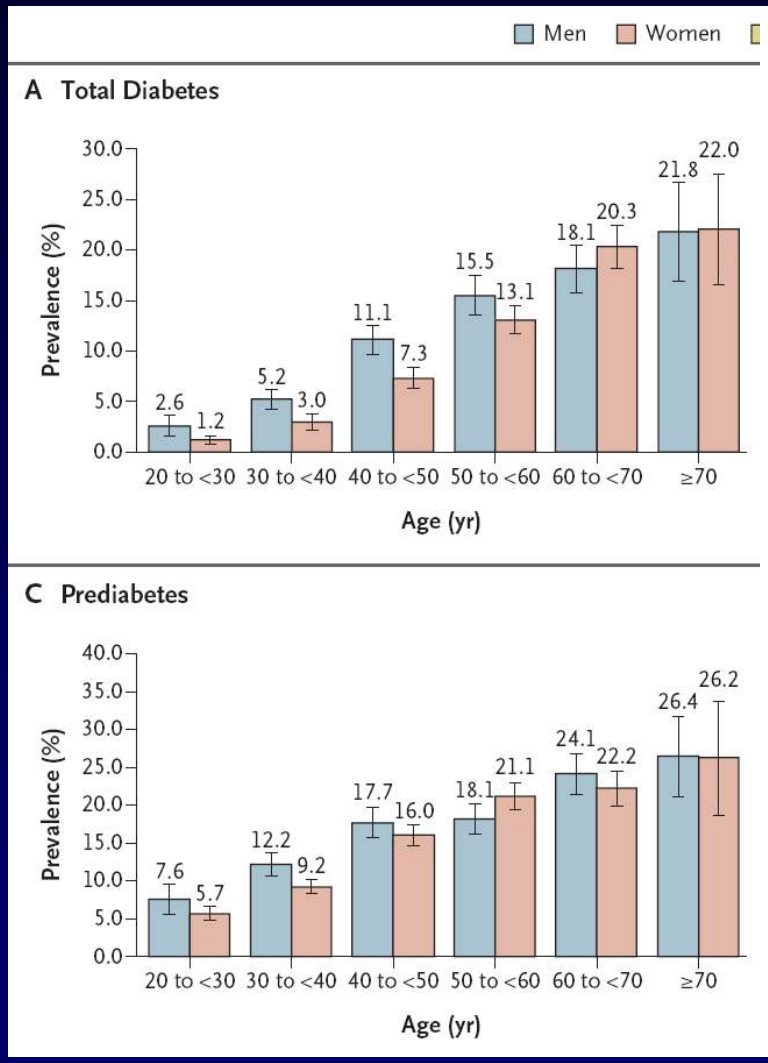
46,239 adults
(> age of 20 years)

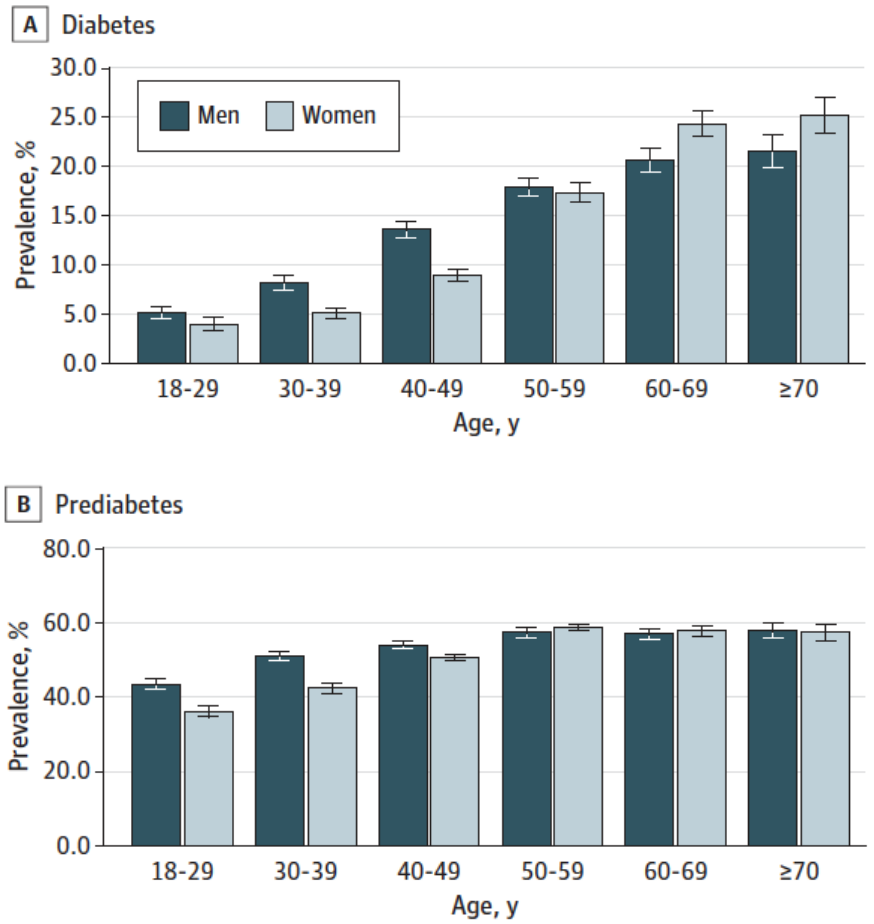
9.7% diabetes
15.5% Prediabetes

92.4 million DM
148.2m Prediabetes

Yang W et al, NEJM 2010; March 25

Evolving Epidemic of Diabetes and Pre-diabetes

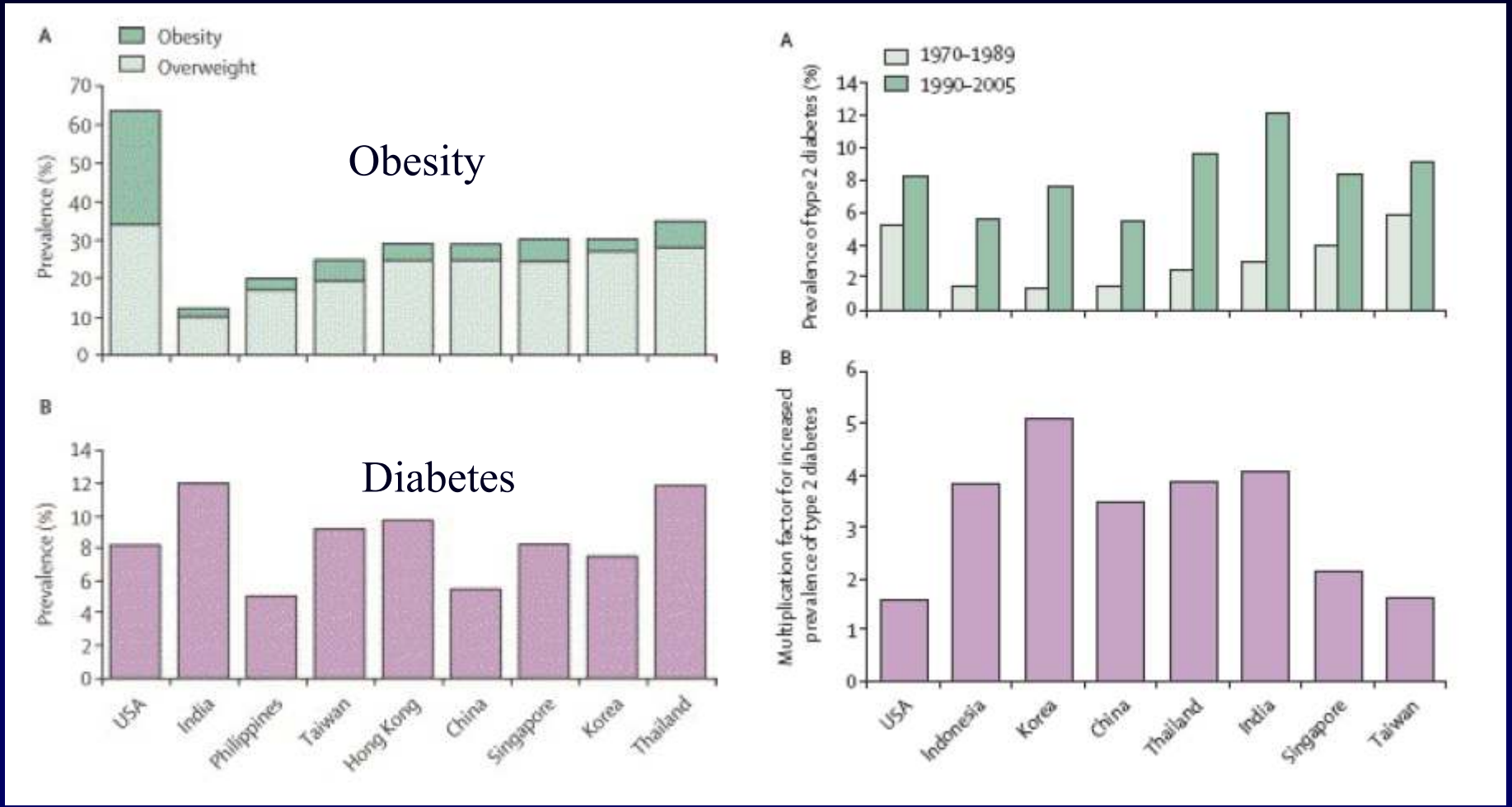




Yang W et al, NEJM 2010; March 25

Xu et al, J Am Med Asso 2013; Sept 4

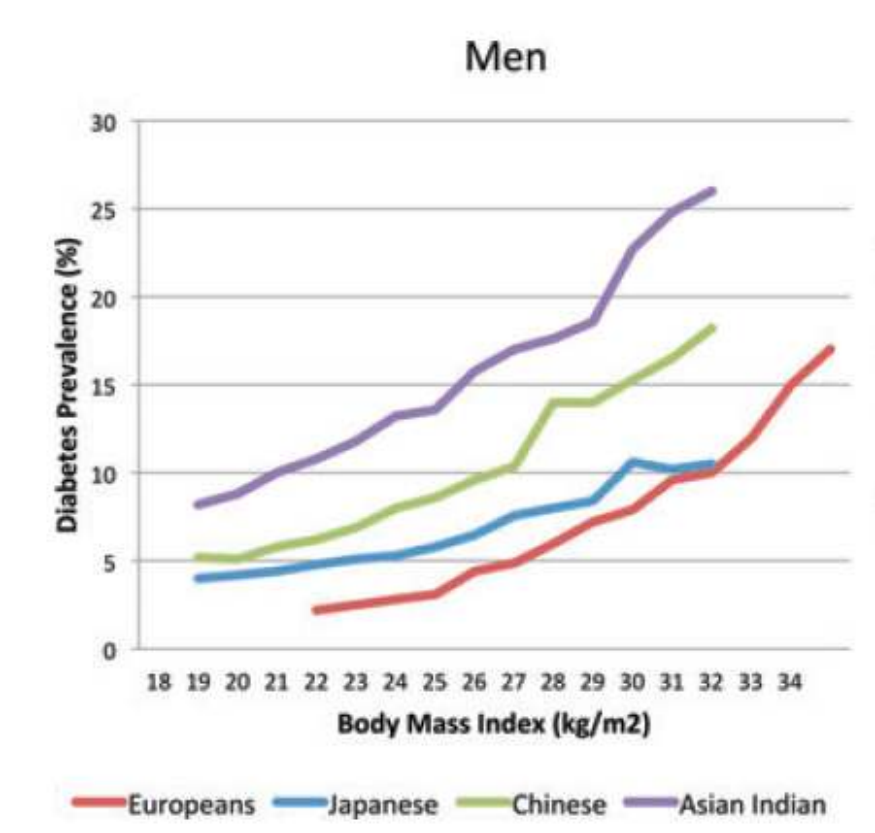
Disparity between prevalance of diabetes and obesity in Asia

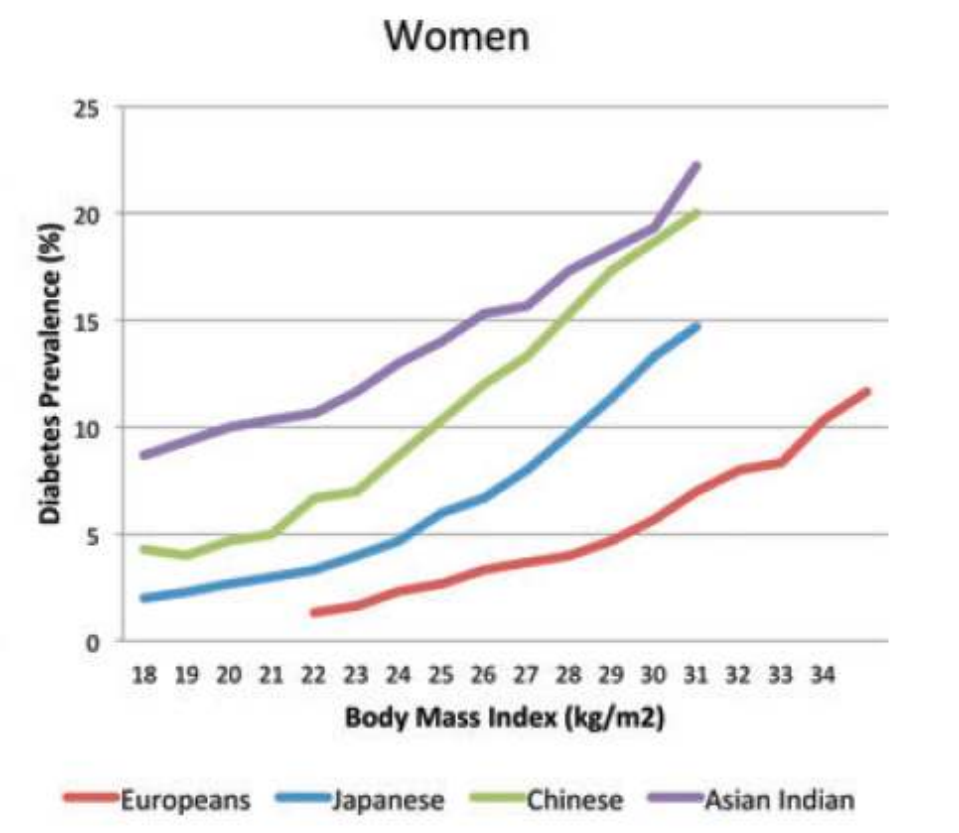


Young onset, strong FH, central obesity

Yoon KH et al, Lancet 2006
Chan JC et al, JAMA 2009

Asians develop T2DM at lower BMI





DECODA Study group: 24,515 M, 29,952 F

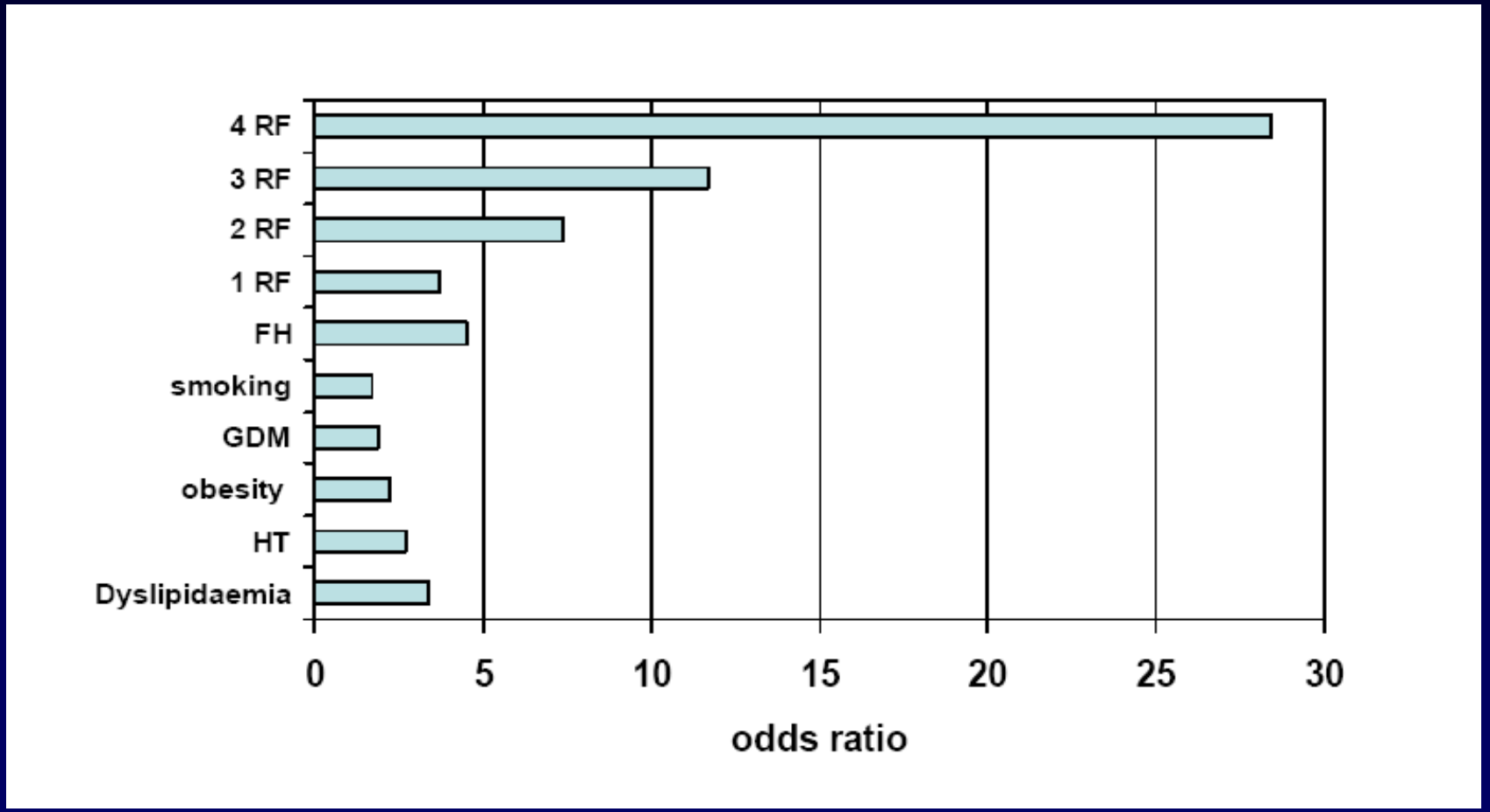
Adapted from Nyamdorj R et al, Int J Obes 2010; 43: 332-9

Country	Diabetes prevalence in 2011 (%)	Estimated number of people affected in 2011	Proportion of DM subjects aged 20–39 in 2011 (%)	Estimated proportion of DM cases undiagnosed in 2011 (%)	IGT prevalence in 2011 (%)	Mean diabetes-related expenditure per person with DM (USD)
China	9.29	90,045,980	15.1	56.9	2.41[a]	194
Hong Kong	9.38	525,390	7.4	46.7	14.87	2,059
Macau	7.49	32,710	10.0	46.7	5.69	480
Taiwan	9.59	1,664,540	9.59	46.7	11.61	1,314
Mongolia	6.74	117,460	43.6	56.9	7.86	107
Japan	11.2	10,674,320	5.9	46.7	14.3	3,266
Dem. People's Republic of Korea	9.08	1,507,500	13.1	63.0	10.83	17
Republic of Korea	8.8	3,186,390	10.0	46.7	13.45	1,615
USA	10.94	23,721,760	13.9	27.7	11.97	8,468
Canada	10.80	2,716,140	6.0	27.7	12.2	5,106
United Kingdom	6.84	3,063,910	6.95	36.6	9.19	4,267
Australia	8.10	1,292,090	8.46	46.7	9.94	4,878

NOTE: the data source is based on projections from epidemiological surveys. Data source: Diabetes Atlas, Fifth edition, 2011. International Diabetes Federation.[1]

[a]IGT prevalence figures reported in the above reference is markedly different to that reported in a recent nationwide study, which reported age-standardized prevalence of diabetes of 9.7%, and 15.5% for prediabetes, including 11.9% with IGT.

Risk factors for DM in Chinese: Insights from epidemiological studies in HK



1649 adults with RF for DM
All underwent 75g OGTT, 15% T2 DM

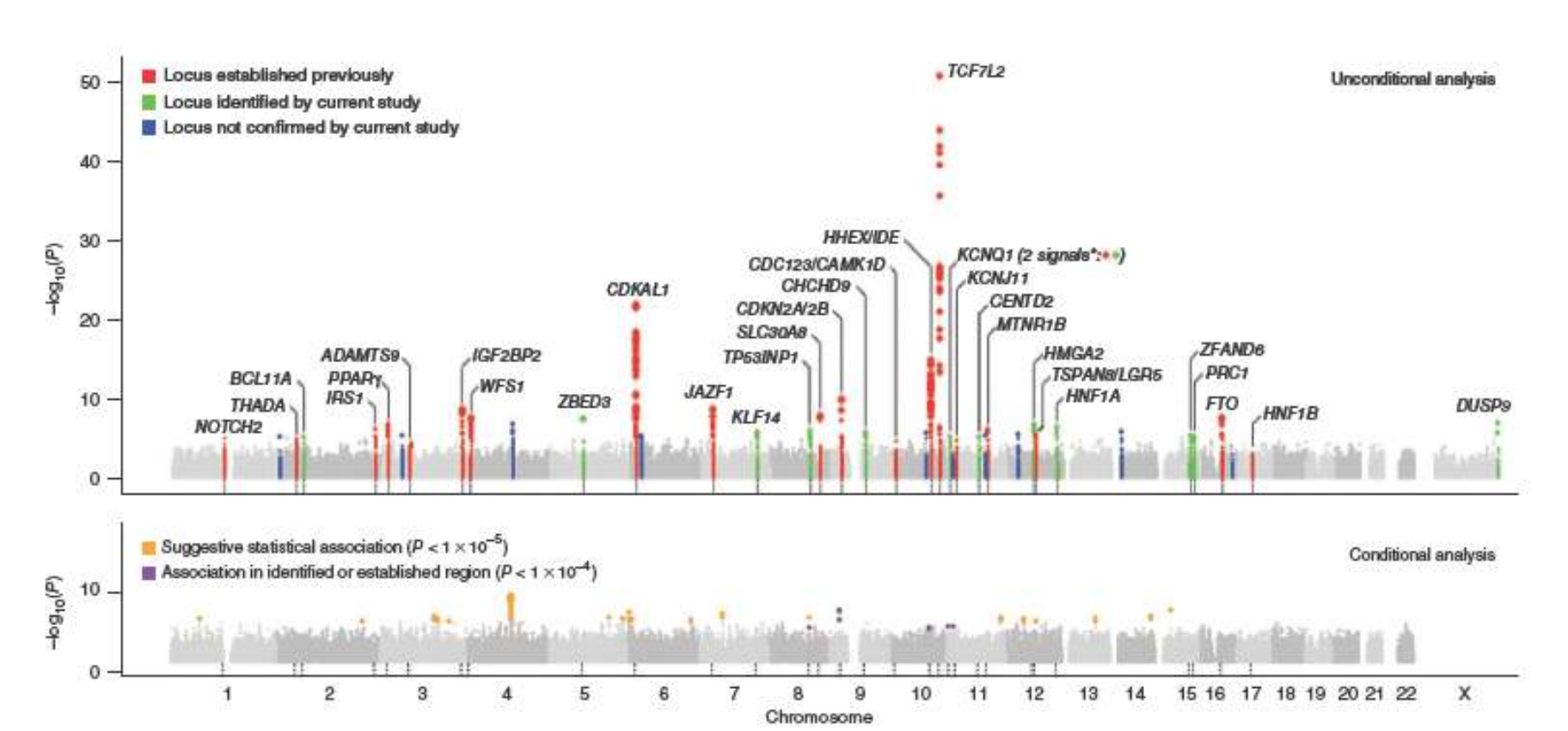
Ko GT et al, Diabetes Care 2000

Family history as most important risk factor in DM in Chinese

Variable	Total Diabetes		Prediabetes	
	Odds Ratio (95% CI)	P Value	Odds Ratio (95% CI)	P Value
Male sex	1.26 (1.12–1.43)	<0.001	1.06 (0.95–1.17)	0.30
Age, per 10-yr increment	1.68 (1.60–1.77)	<0.001	1.37 (1.31–1.45)	<0.001
Family history of diabetes	3.14 (2.68–3.68)	<0.001	1.32 (1.12–1.56)	0.001
Less than college education	1.57 (1.34–1.84)	<0.001	1.17 (1.03–1.33)	0.02
Overweight†	1.43 (1.22–1.67)	<0.001	1.42 (1.25–1.62)	<0.001
Obesity‡	2.17 (1.68–2.81)	<0.001	2.05 (1.66–2.54)	<0.001
Central obesity§	1.39 (1.18–1.63)	<0.001	1.22 (1.06–1.40)	0.006
Heart rate, per increase of 10 beats/min	1.29 (1.21–1.36)	<0.001	1.15 (1.09–1.21)	<0.001
Systolic blood pressure, per increase of 10 mm Hg	1.17 (1.13–1.20)	<0.001	1.12 (1.09–1.15)	<0.001
Triglycerides, per increase of 50 mg/dl (0.56 mmol/liter)	1.28 (1.22–1.33)	<0.001	1.20 (1.16–1.25)	<0.001
Urban residence	1.22 (1.08–1.38)	0.002	0.90 (0.81–0.99)	0.04

Yang W et al, NEJM March 2010

Identified genetic variants for T2 DM



Gene regions as of Sept 2012: >60

Voigt B et al, Nature Genetics 2010

Frequency and effect size of variants in Asians vs Europeans

Nearby gene	SNP	Risk Allele	European T2D N=55,826		Korean T2D N=1393		Korean GDM N=1501	
			Control risk AF	OR	Control risk AF	OR	Control risk AF	OR
CDKAL1	Rs7756992	G	0.26	1.20	0.53	1.26	0.53	1.39
	Rs7754840	C	0.31	1.12	0.46	1.24	0.46	1.55
CDKN2A/2B	Rs10811661	T	0.83	1.20	0.51	1.55	0.51	1.49
FTO	Rs8050136	A	0.39	1.17	0.12	1.15	0.12	1.12
HHEX	Rs1111875	C	0.53	1.13	0.31	1.21	0.31	1.27
	Rs7923837	G	0.62	1.22	0.21	1.33	0.21	1.26
IGFBP2	Rs4402960	T	0.29	1.14	0.30	1.18	0.30	1.18
SLC30A8	Rs13266634	C	0.65	1.12	0.59	1.18	0.59	1.24
TCF7L2	Rs7903146	T	0.26	1.37	0.03	1.53	0.03	1.58

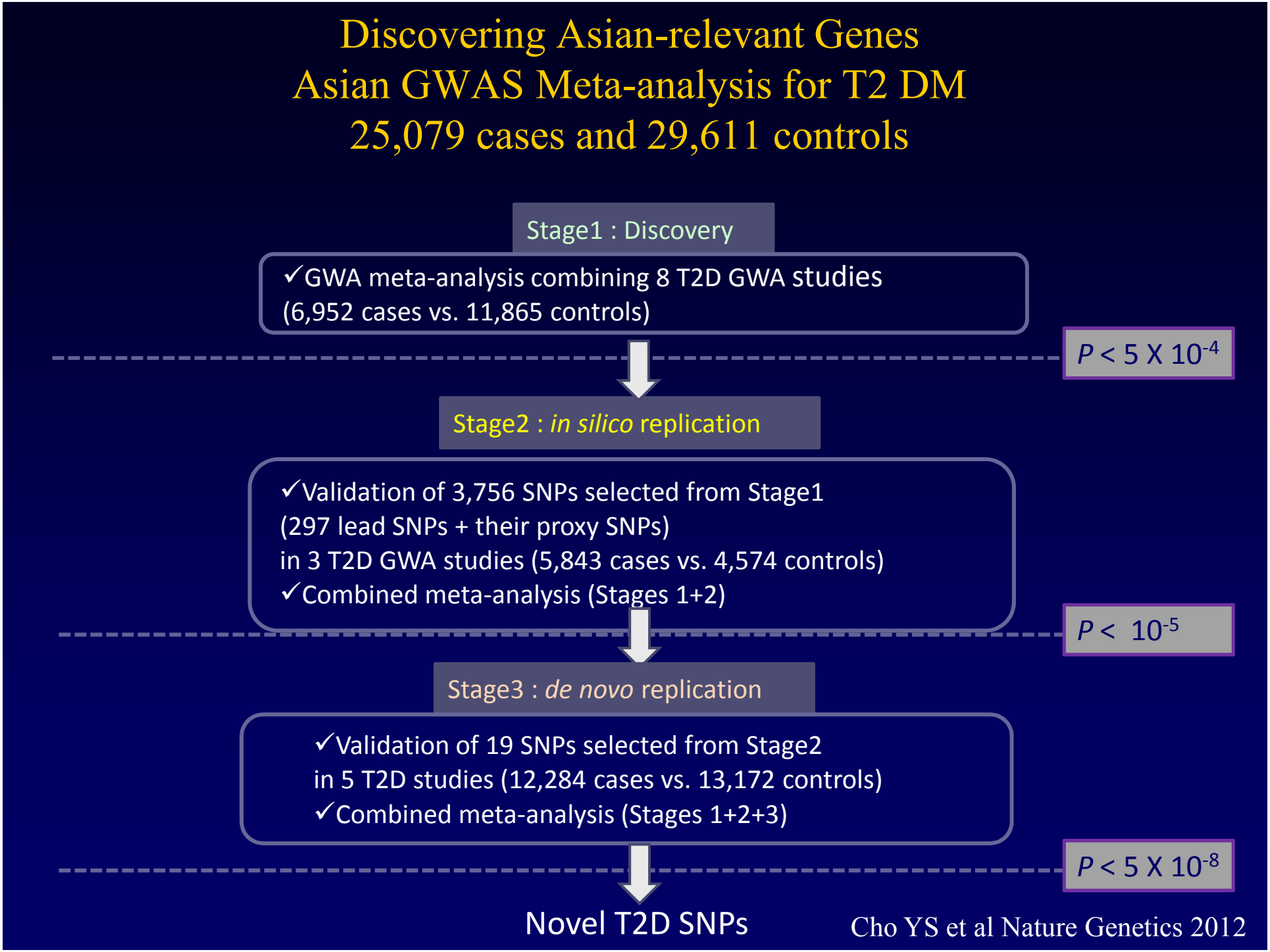
Cho YM et al, Diabetologia 2009

Genetic markers in E. Asians vs Europeans

> 60 variants discovered

Ma RC and Chan JC, *Annals NY Acad Sci 2013*

Discovering Asian-relevant Genes
Asian GWAS Meta-analysis for T2 DM
25,079 cases and 29,611 controls



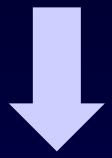
Cho YS et al Nature Genetics 2012

Eight novel loci all implicated in beta cell development and protein metabolism

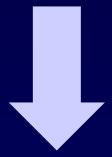
SNP	chr	Loci	Risk allele	OR (CI)	P-value	Possible functions
rs6815464	4	*MAEA*	c	1.13 (1.10-1.16)	1.57E-20	erythroblast enucleation & macrophages maturation
rs7041847	9	*GLIS3*	a	1.10 (1.07-1.13)	1.99E-14	beta cell development and insulin expression
rs6017317	20	*FITM2-R3HDML-HNF4A*	g	1.09(1.07-1.12)	1.12E-11	pancreatic islet development
rs6467136	7	*GCC1*	g	1.11 (1.07-1.14)	4.96E-11	organization of the trans-Golgi network
rs831571	3	*PSMD6*	c	1.09 (1.06-1.12)	8.41E-11	degradation of ubiquitinated proteins
rs9470794	6	*ZFAND3*	c	1.12 (1.08-1.16)	2.06E-10	zinc finger transcription factor
rs3786897	19	*PEPD*	a	1.10 (1.07-1.14)	1.30E-08	Beta cell development
rs1535500	6	*KCNK16*	t	1.08 (1.05-1.11)	2.30E-08	defective regulation of potassium channel activity

Identification of novel T2D loci in Chinese

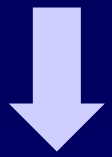
Stage 1: Meta-analysis of GWAS in Chinese
684 T2 DM cases: 955 controls



Stage 2: *de novo* replication in Chinese
11067 T2 DM: 7929 controls

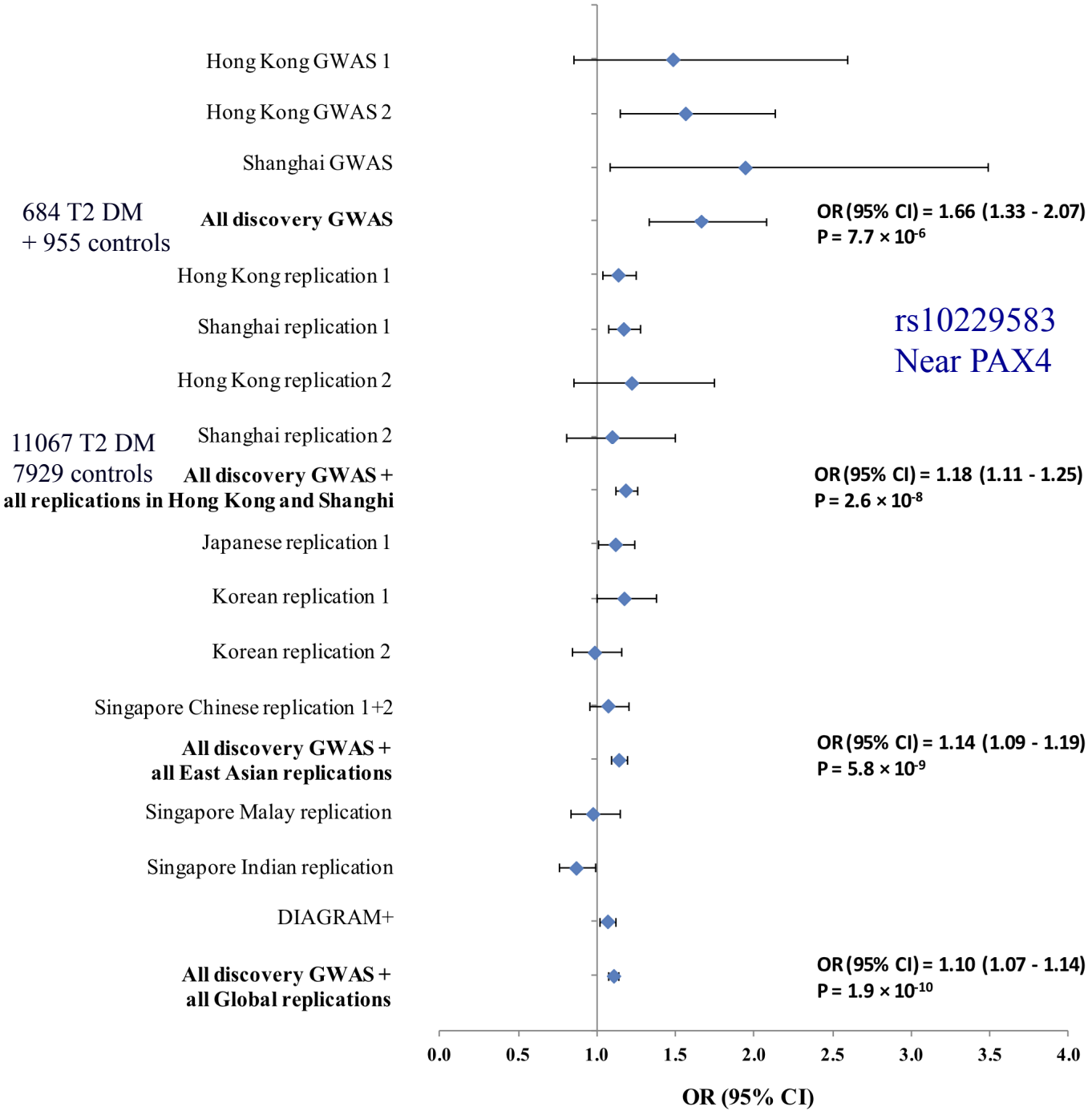


Stage 3: *in silico* replication in East Asians
8700 T2 DM: 9216 controls



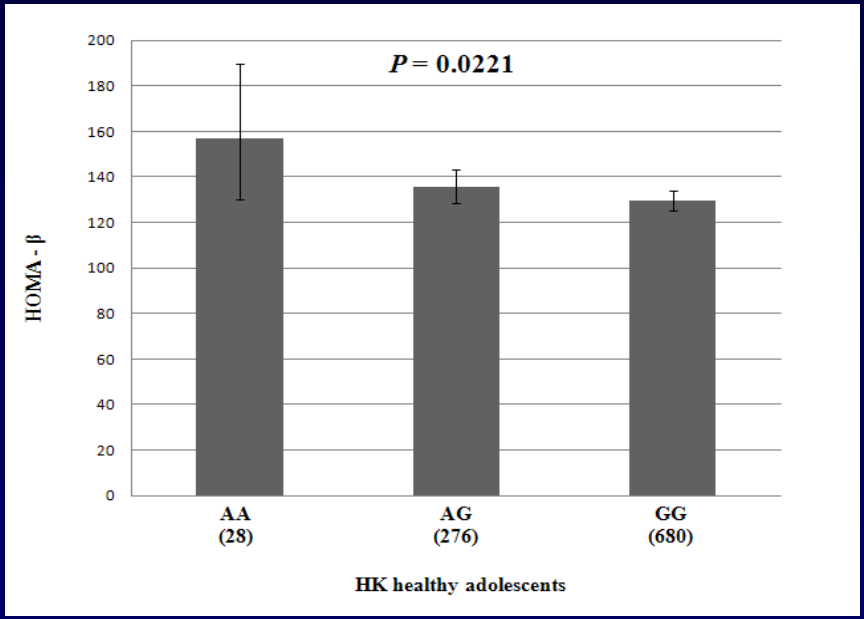
Stage 4*: in silico* replication in other populations
9901 T2 DM: 41360 controls

Global meta-analysis of stages 1+2+3+4
29668 cases: 58505 controls

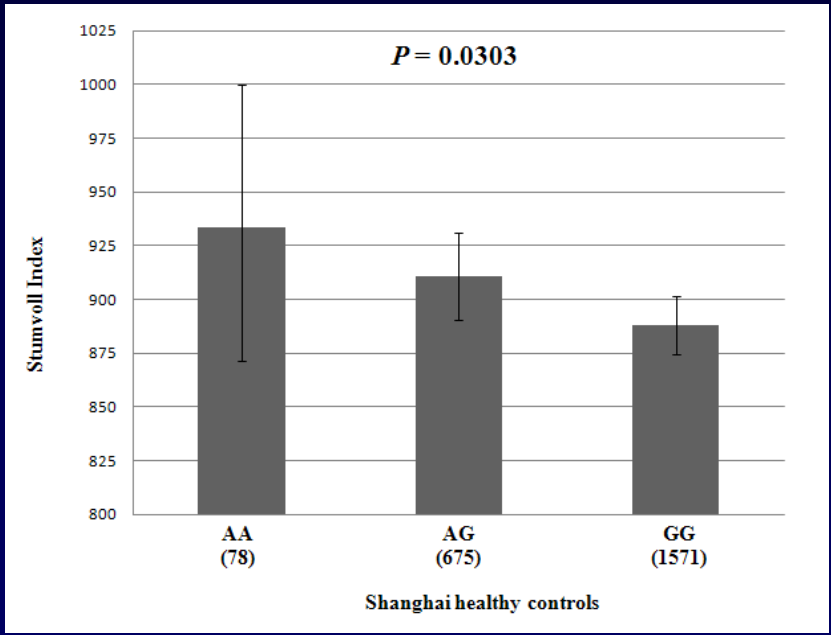

Hong Kong GWAS 1
Hong Kong GWAS 2
Shanghai GWAS
684 T2 DM
+ 955 controls
All discovery GWAS
OR (95% CI) = 1.66 (1.33 - 2.07)
P = 7.7 × 10-6
Hong Kong replication 1
Shanghai replication 1
rs10229583
Near PAX4
Hong Kong replication 2
Shanghai replication 2
11067 T2 DM
7929 controls
All discovery GWAS +
all replications in Hong Kong and Shanghi
OR (95% CI) = 1.18 (1.11 - 1.25)
P = 2.6 × 10-8
Japanese replication 1
Korean replication 1
Korean replication 2
Singapore Chinese replication 1+2
All discovery GWAS +
all East Asian replications
OR (95% CI) = 1.14 (1.09 - 1.19)
P = 5.8 × 10-9
Singapore Malay replication
Singapore Indian replication
DIAGRAM+
All discovery GWAS +
all Global replications
OR (95% CI) = 1.10 (1.07 - 1.14)
P = 1.9 × 10-10
0.0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
OR (95% CI)

Novel variant predicts impaired beta-cell function in Chinese

Healthy adolescents HK

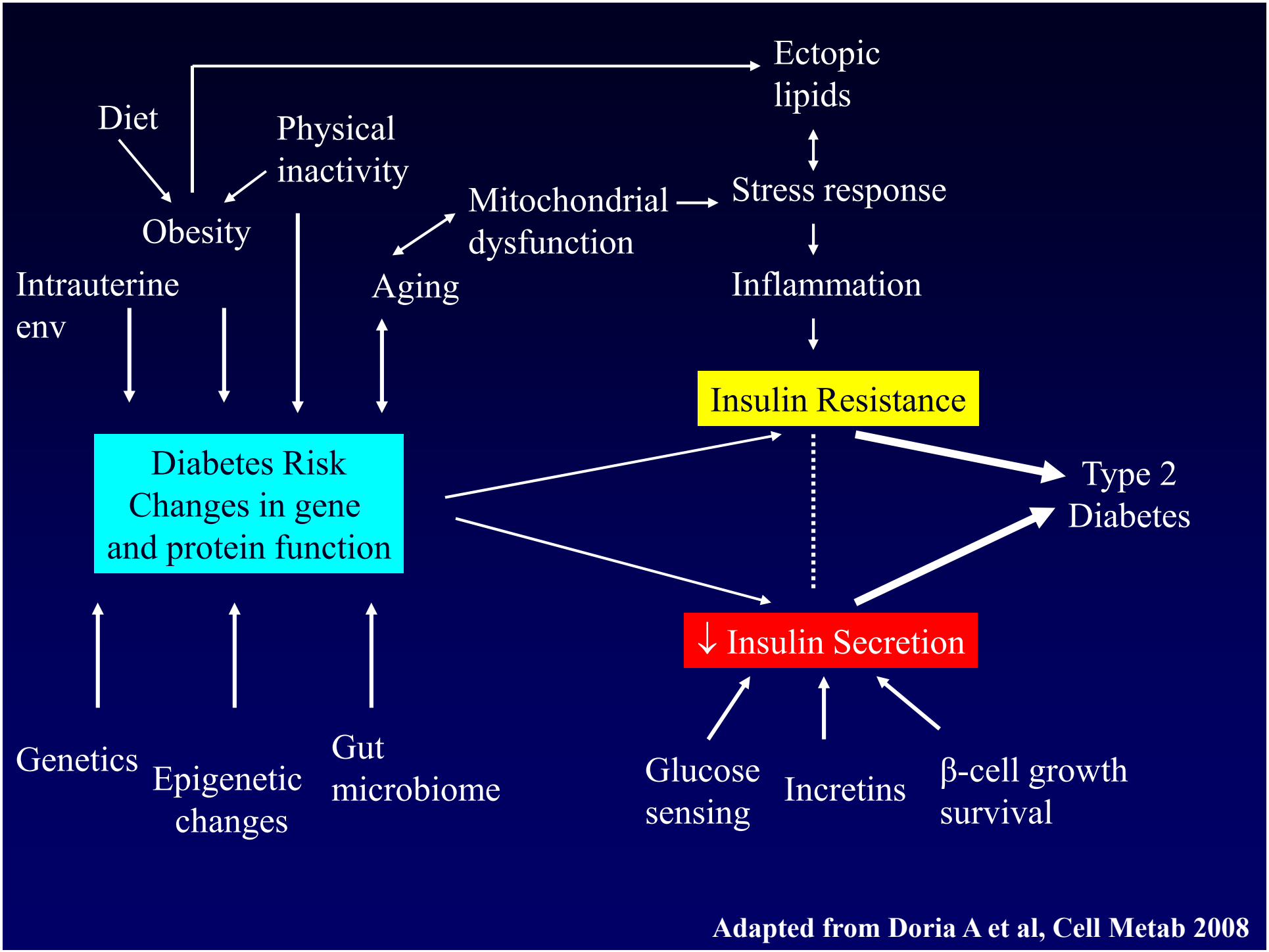


Shanghai healthy controls

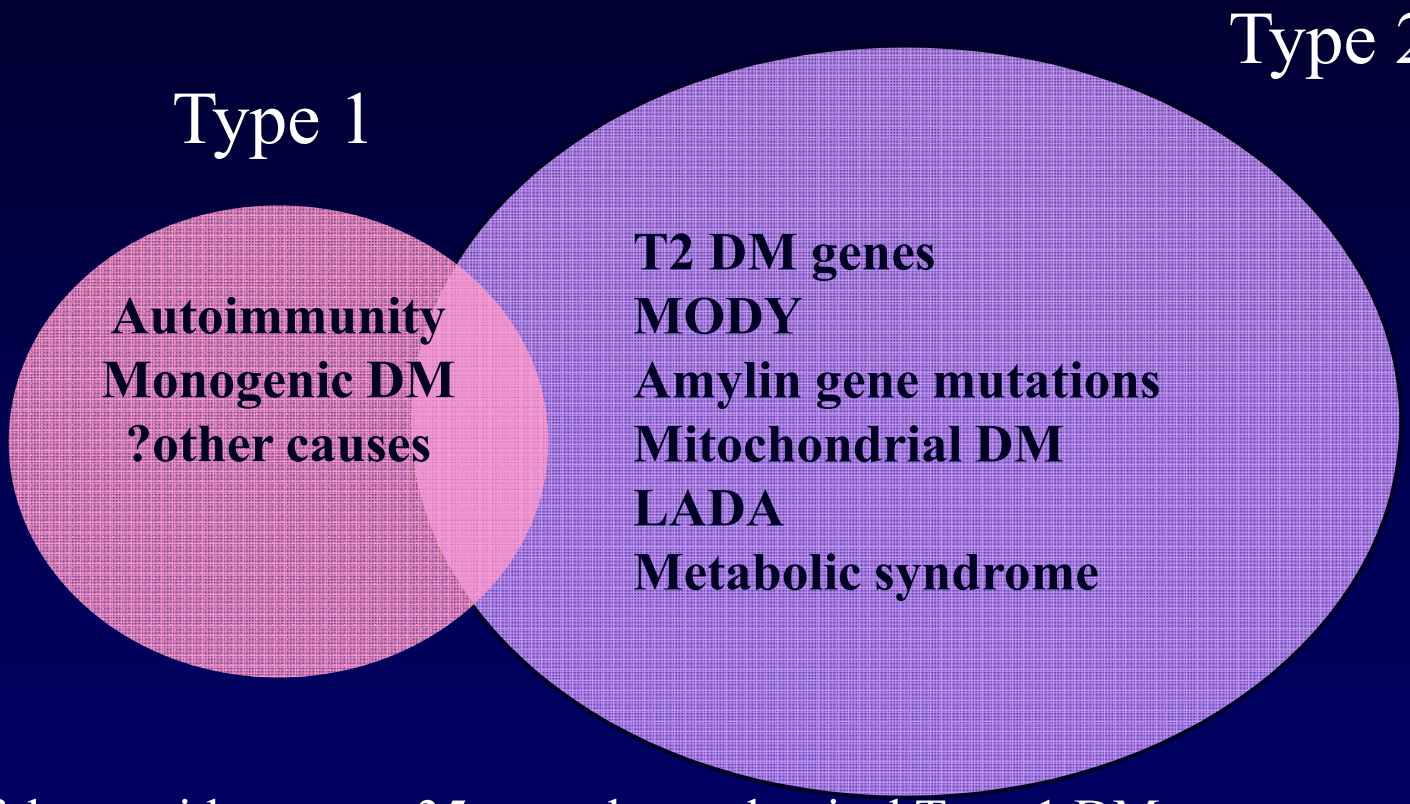


Associated with earlier age of diagnosis:
P=2.3 × 10^{-4}, $\beta_{unadjusted}$ ± SE = -0.90 ± 0.24)

Ma RC, Hu C et al, Diabetologia 2013, March 27


Ectopic lipids
Diet
Physical inactivity
Obesity
Mitochondrial dysfunction
Stress response
Intrauterine env
Aging
Inflammation
Insulin Resistance
Diabetes Risk
Changes in gene and protein function
Type 2 Diabetes
↓ Insulin Secretion
Genetics
Epigenetic changes
Gut microbiome
Glucose sensing
Incretins
β-cell growth survival
Adapted from Doria A et al, Cell Metab 2008

Heterogeneity of DM in Asian populations



Only 10% of those with onset < 35 years have classical Type 1 DM

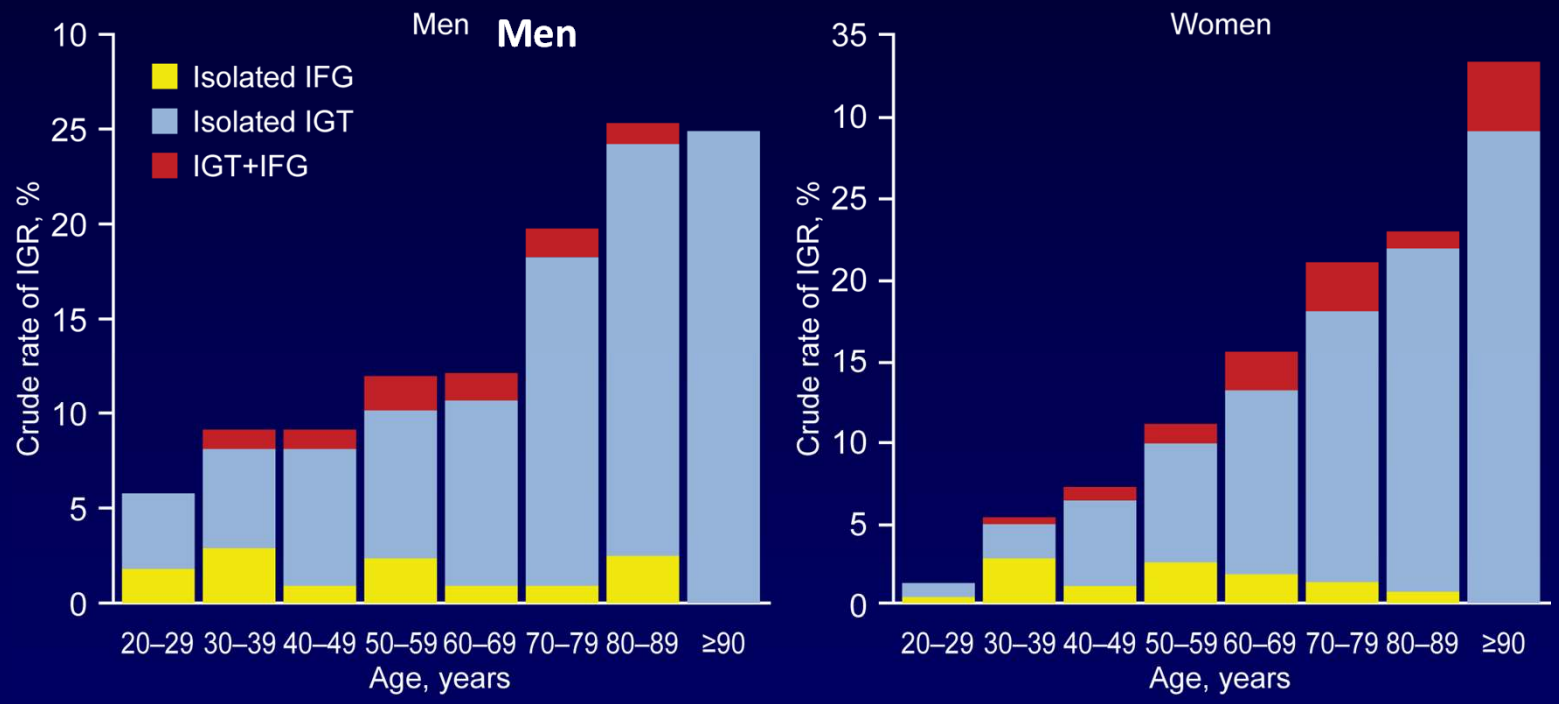
30-50% are insulin resistant

In young-onset T2 DM, 10-15% carry either genetic or markers of insulin deficiency

Anti-GAD present in 31% of T1DM, 11.8% of normal wt T2DM, 2.9% of obese T2DM

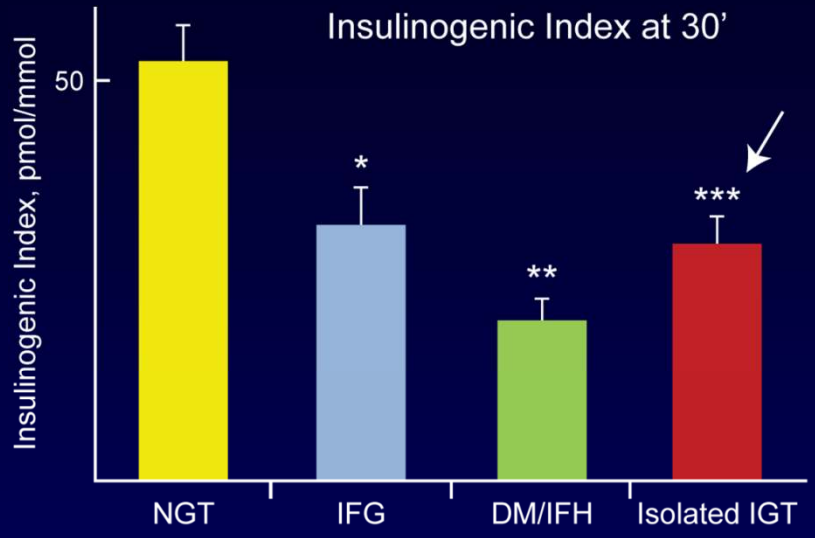
Chan JC et al, JAMA 2009

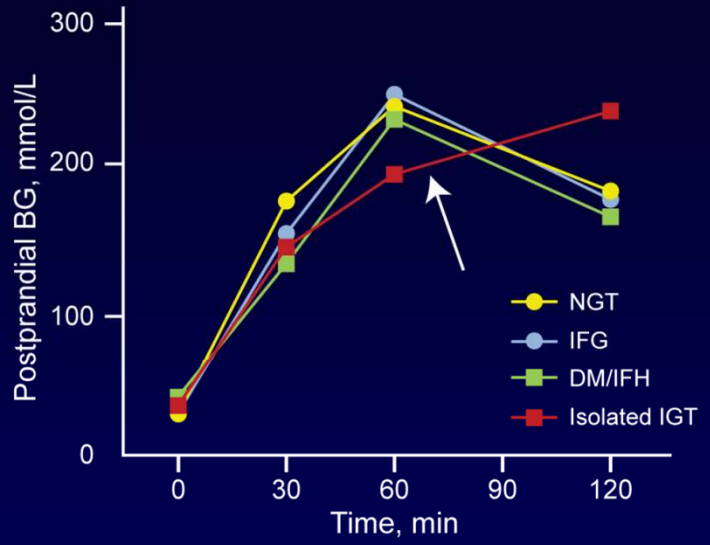
Shanghai Diabetes Survey (1998–2000)
Most Subjects with Pre-diabetes have IGT

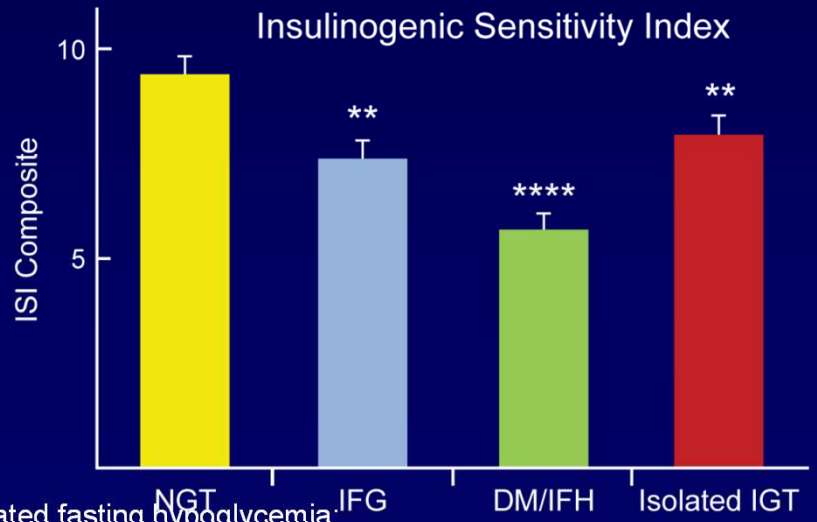


IFG=impaired fasting plasma glucose (>5.6 to 7 mmol/L); IGR=impaired glucose regulation; IGT=impaired glucose tolerance (2-hour postprandial glucose 7.8 to 11.1 mmol/L)
Jia et al. *Diabetologia* 2007;50:286-292

Reduced First-Phase Insulin Secretion in Japanese with Pre-diabetes







DM/IFH=diabetes mellitus with isolated fasting hypoglycemia; IFG=impaired fasting glucose; IGT=impaired glucose tolerance; NGT=normal glucose tolerance

Nishi et al. *Diabetes Res Clin Pract* 2005;70:46-52

Both visceral fat and β-cell function predict diabetes in American Japanese

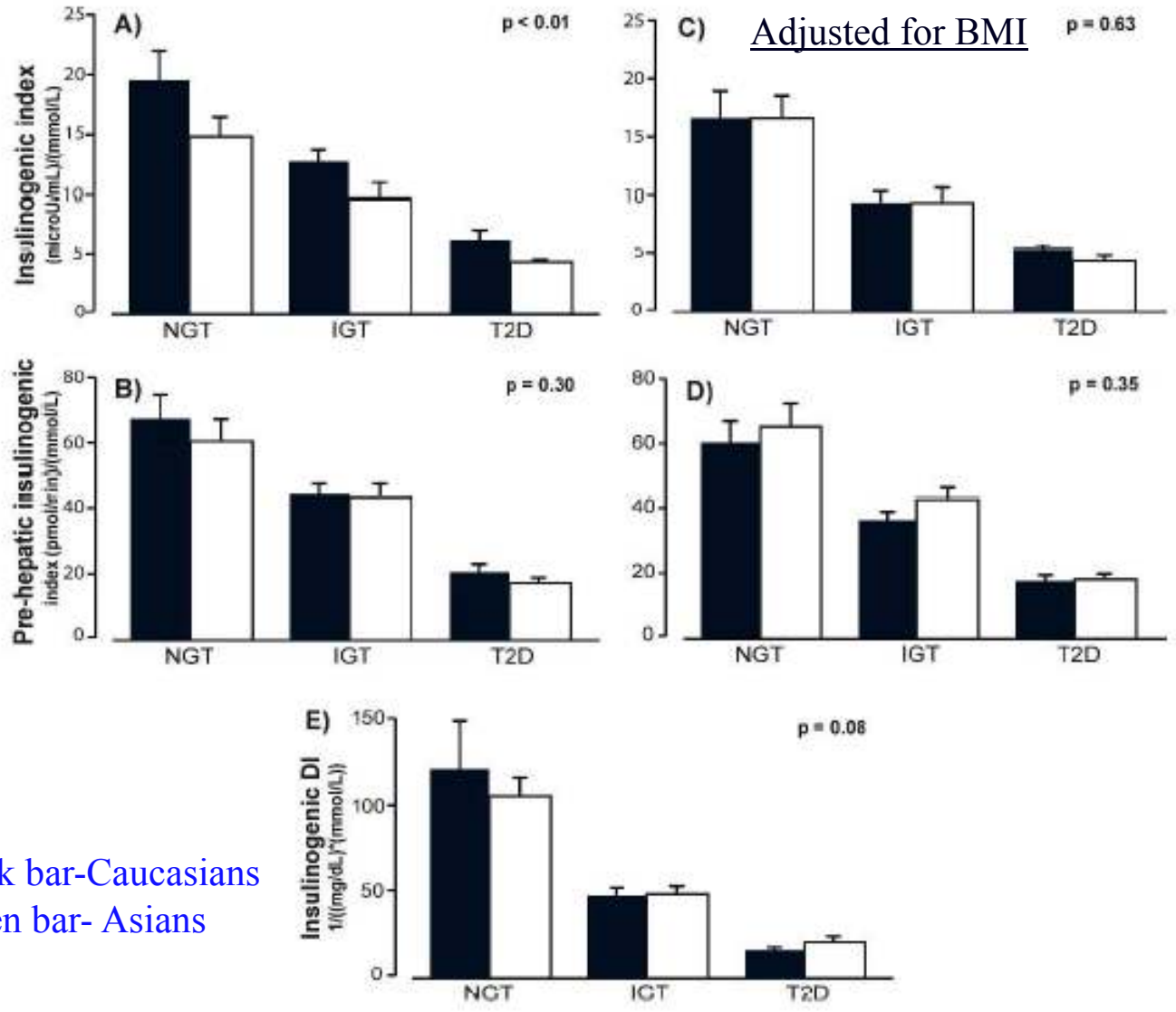
Variables	OR (95% CI)	P-value
Age	1.4 (1.0 – 2.0)	0.065
Female gender	1.8 (0.8 – 4.2)	0.176
IGT at baseline	4.5 (2.3 – 9.0)	<0.001
DM family history	1.9 (1.0 – 3.3)	0.040
Visceral Fat area	1.6 (1.1 – 2.4)	0.023
Body mass index	0.8 (0.5 – 1.2)	0.251
Fasting C-peptide	1.4 (1.1 – 1.8)	0.016
Incremental insulin response	0.5 (0.3 – 0.9)	0.022

Boyko E Diabetes Care 2000

Pathophysiology in Asians vs Caucasians

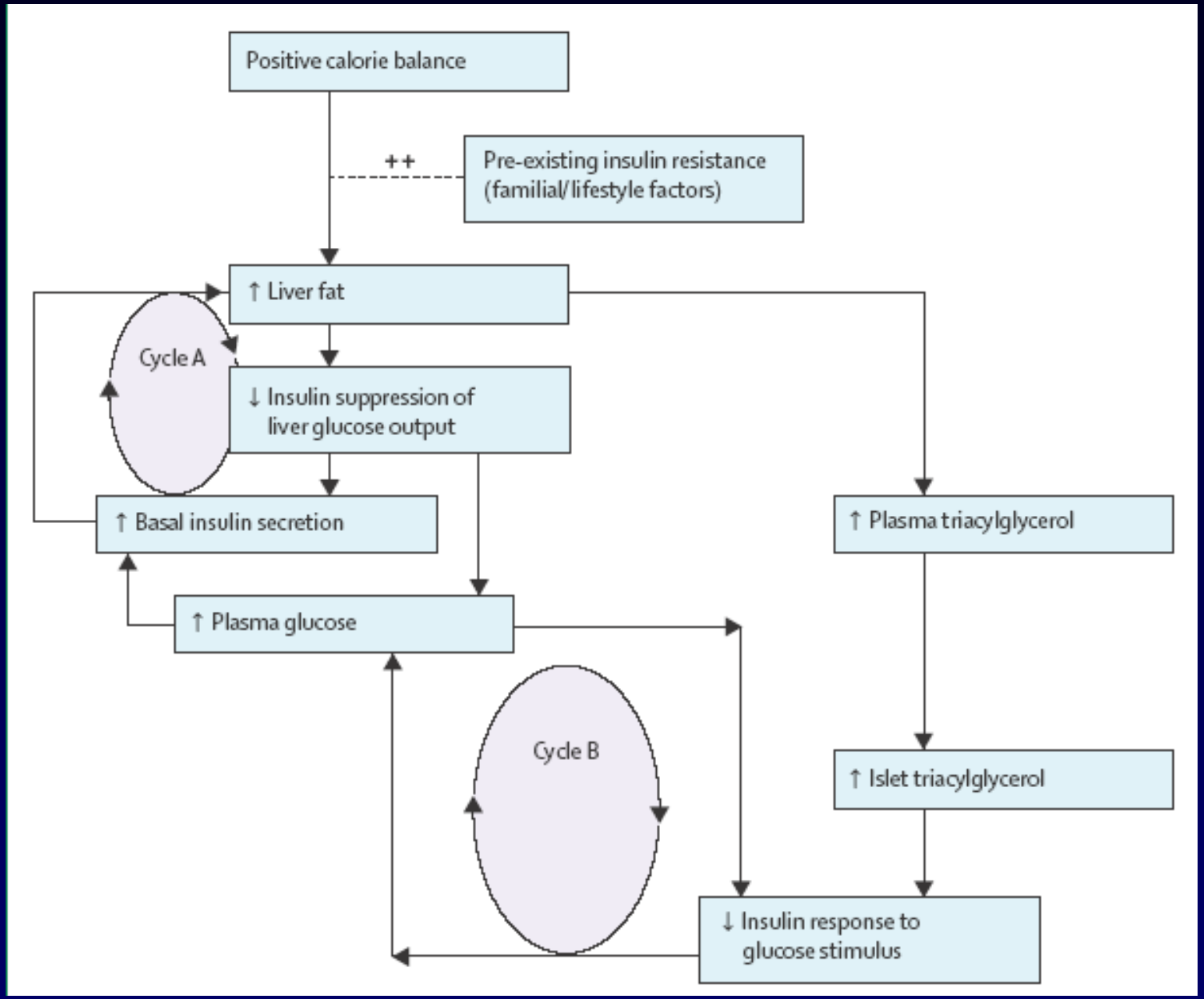
120 Japanese
150 Europeans

Representative
Population aroun
BMI cut-off



Dark bar-Caucasians
Open bar- Asians

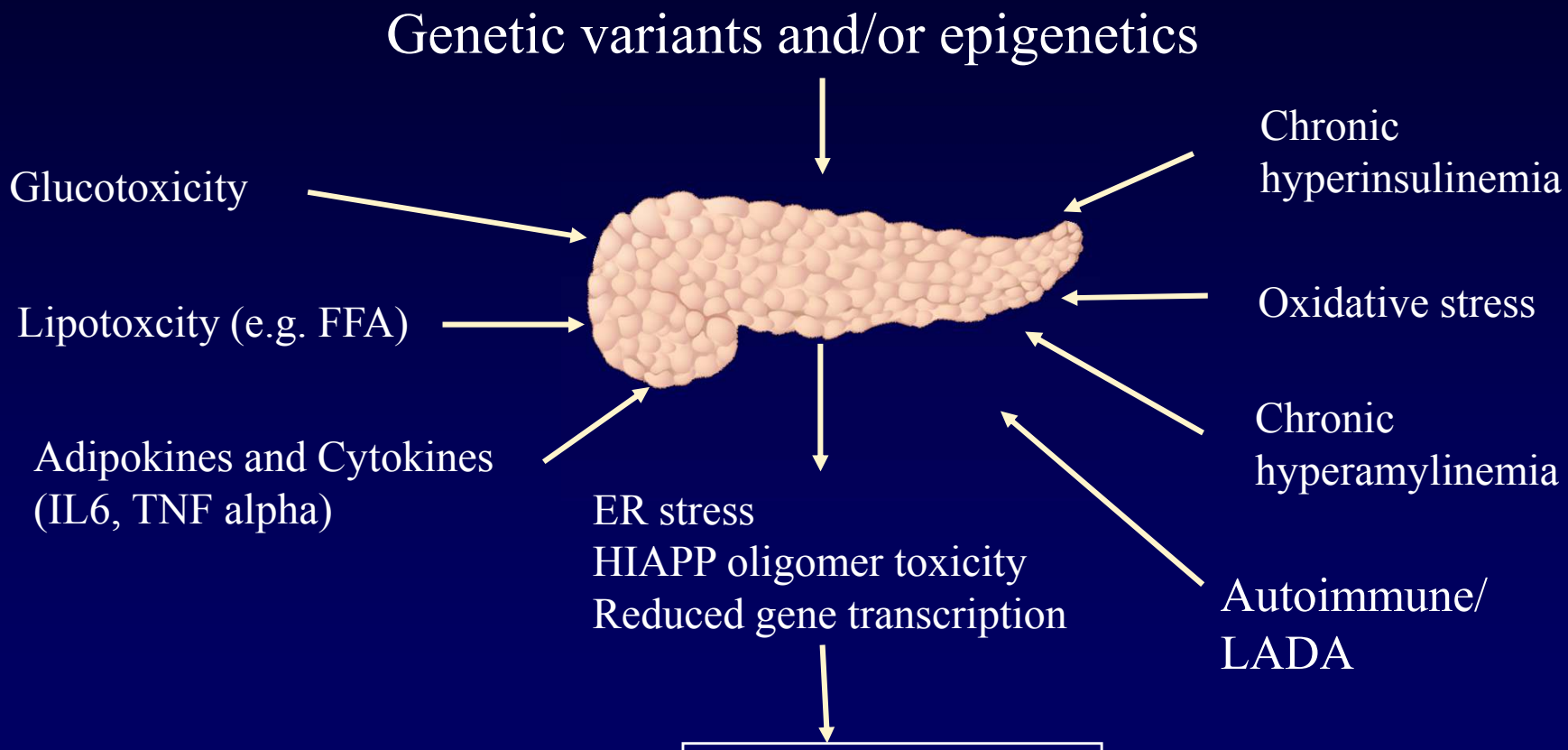
Moller J et al, Diabetes Care 2013; Oct 15



Pathogenesis of Type 2 DM

Taylor R. Diabetologia 2008; 51: 1781-89

Causes of Beta-cell dysfunction

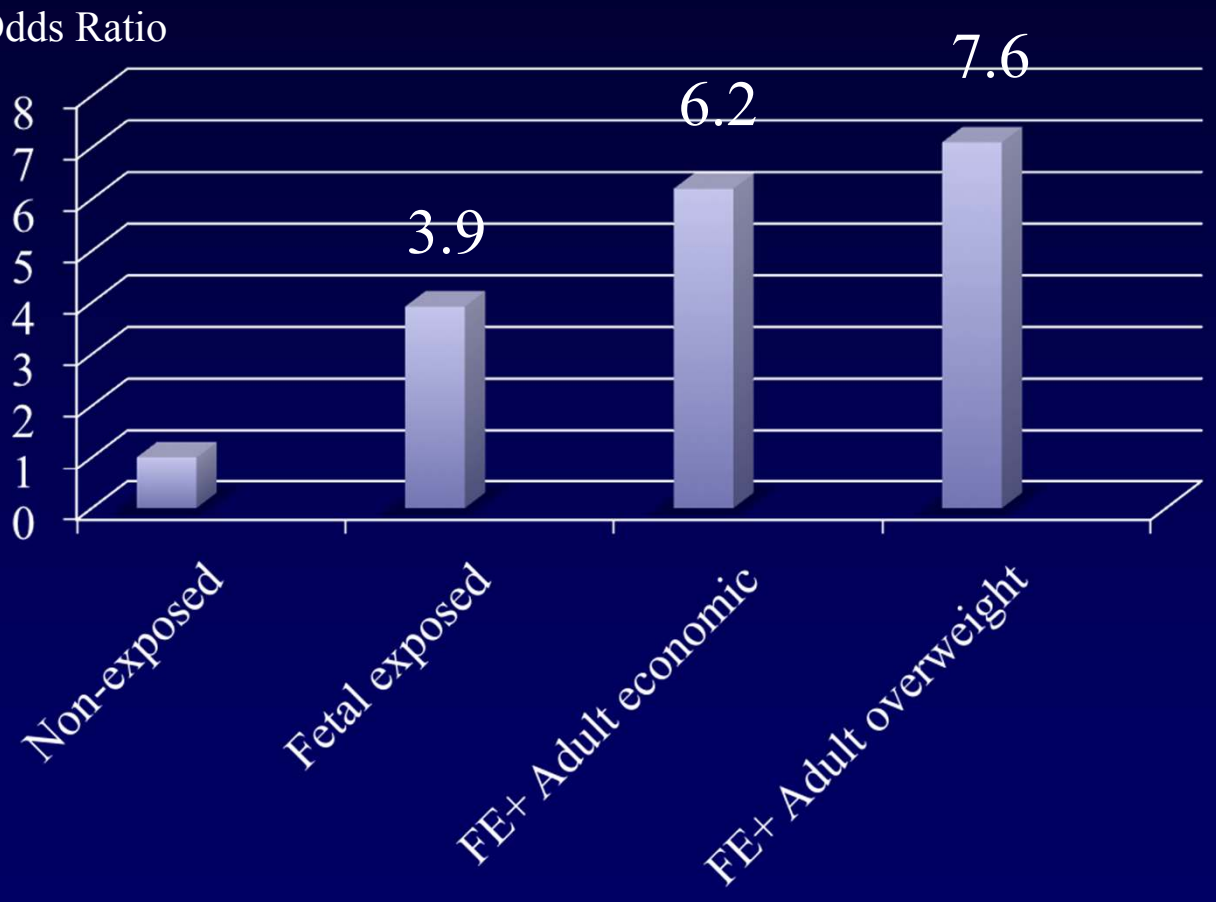


Boden G, Shulman GI. *Eur J Clin Invest*. 2002;32:14-23.
Finegood DT, Topp B. *Diabetes Obes Metab*. 2001
Butler PC et al Endocrine Review 2008;

Exposure to Chinese famine and hyperglycaemia in adults

7,874 rural adults
From China National Nutrition and Health survey
Examined exposure to Chinese famine 1959-61

Risk of hyperglycaemia
OR 3.92



Li Y et al, Diabetes 2010

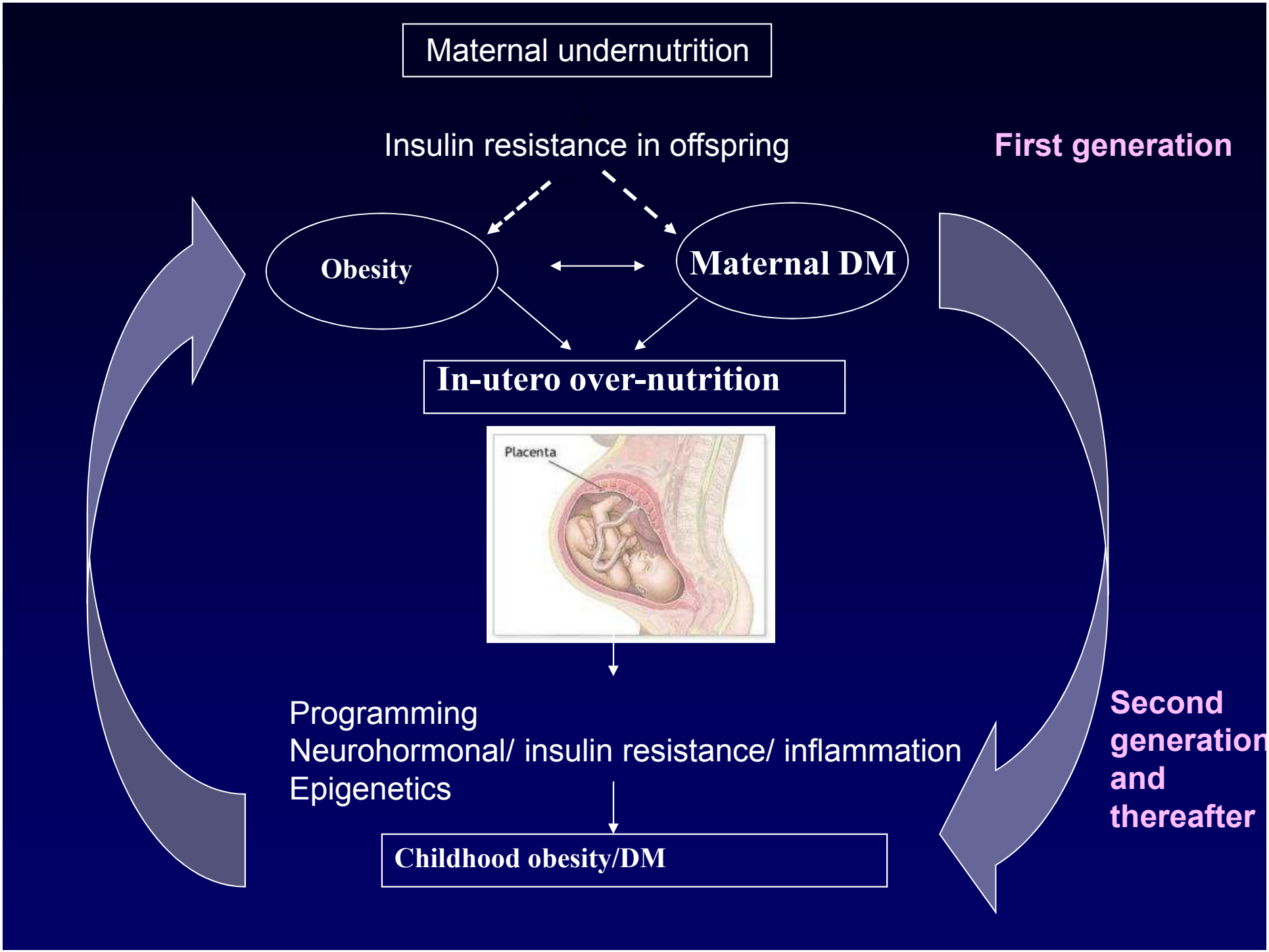
Birthweight and risk of T2DM in Taiwan

1,966 children with T2DM, 1,780 random controls, extract Bwt
429 T2DM, 549 non-DM children

Table 2—*OR for type 2 diabetes by birth weight category in the schoolchildren in Taiwan*

	Birth weight (g) category				
Variable	<2,500	2,500–2,999	3,000–3,499	3,500–3,999	≥4,000
n (case/control)	23/17	71/90	153/262	115/137	67/43
Crude OR	2.32 (1.20–4.47)	1.35 (0.93–1.96)	1.00	1.43 (1.05–1.98)	2.67 (1.73–4.11)
OR (95% CI of diabetes) after adjustment for:					
Age	2.30 (1.19–4.44)	1.34 (0.93–1.95)	1.00	1.42 (1.04–1.96)	2.67 (1.73–4.11)
Age and sex	2.27 (1.17–4.39)	1.35 (0.93–1.95)	1.00	1.42 (1.03–1.96)	2.61 (1.69–4.02)
Age, sex, and BMI	2.38 (1.12–5.06)	1.47 (0.94–2.29)	1.00	1.30 (0.89–1.90)	2.06 (1.25–3.40)
Age, sex, BMI, and family history of diabetes	2.17 (1.00–4.75)	1.41 (0.89–2.22)	1.00	1.15 (0.77–1.72)	1.79 (1.06–3.02)
Age, sex, BMI, family history of diabetes, and SES	2.91 (1.25–6.76)	1.41 (0.89–2.25)	1.00	1.19 (0.79–1.78)	1.78 (1.04–3.06)
Age, sex, BMI, family history of diabetes, SES, and GDM	2.87 (1.19–6.92)	1.46 (0.90–2.38)	1.00	1.18 (0.76–1.83)	1.64 (0.91–2.96)

Wei JN et al, Diabetes Care 2003 343-8;

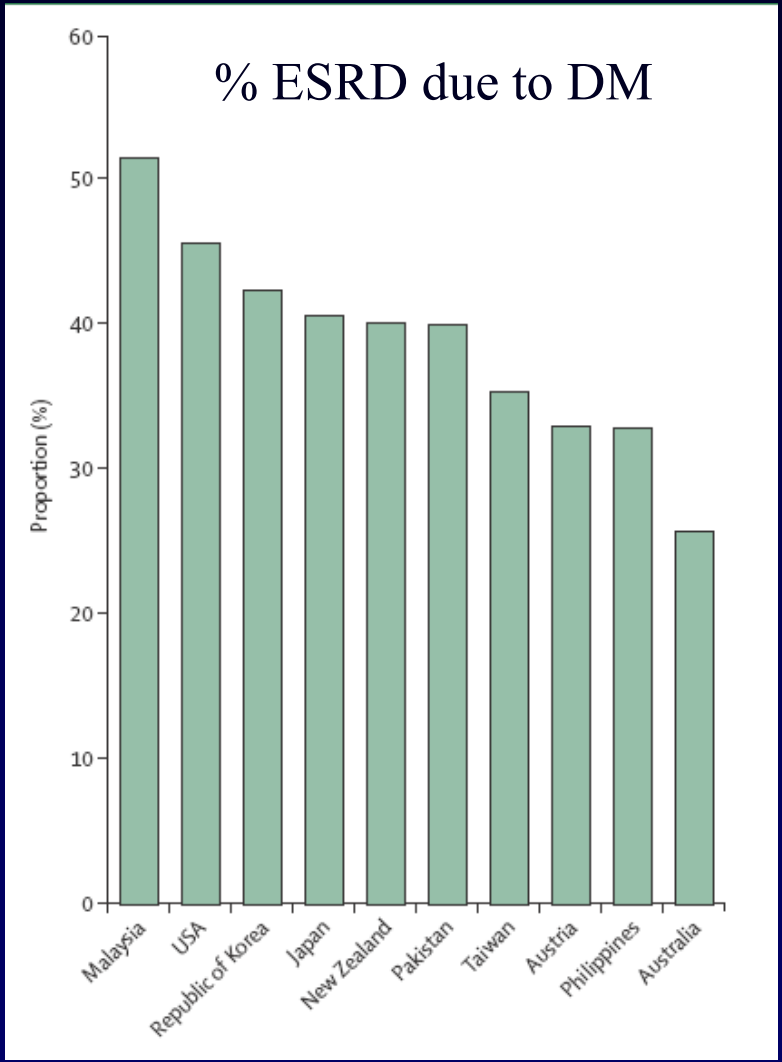

Maternal undernutrition
Insulin resistance in offspring
First generation
Obesity
Maternal DM
In-utero over-nutrition
Placenta
Programming
Neurohormonal/ insulin resistance/ inflammation
Epigenetics
Childhood obesity/DM
Second generation and thereafter

Outline

- Epidemiology of Diabetes in Asia
- Familial young-onset DM
- Genetic predictors of T2DM in E. Asians
- Pathophysiology and role of beta-cell dysfunction
- Pattern of DM complications
- Impact of gestational diabetes
- Implications for treatment and prevention

High prevalence of Renal Disease

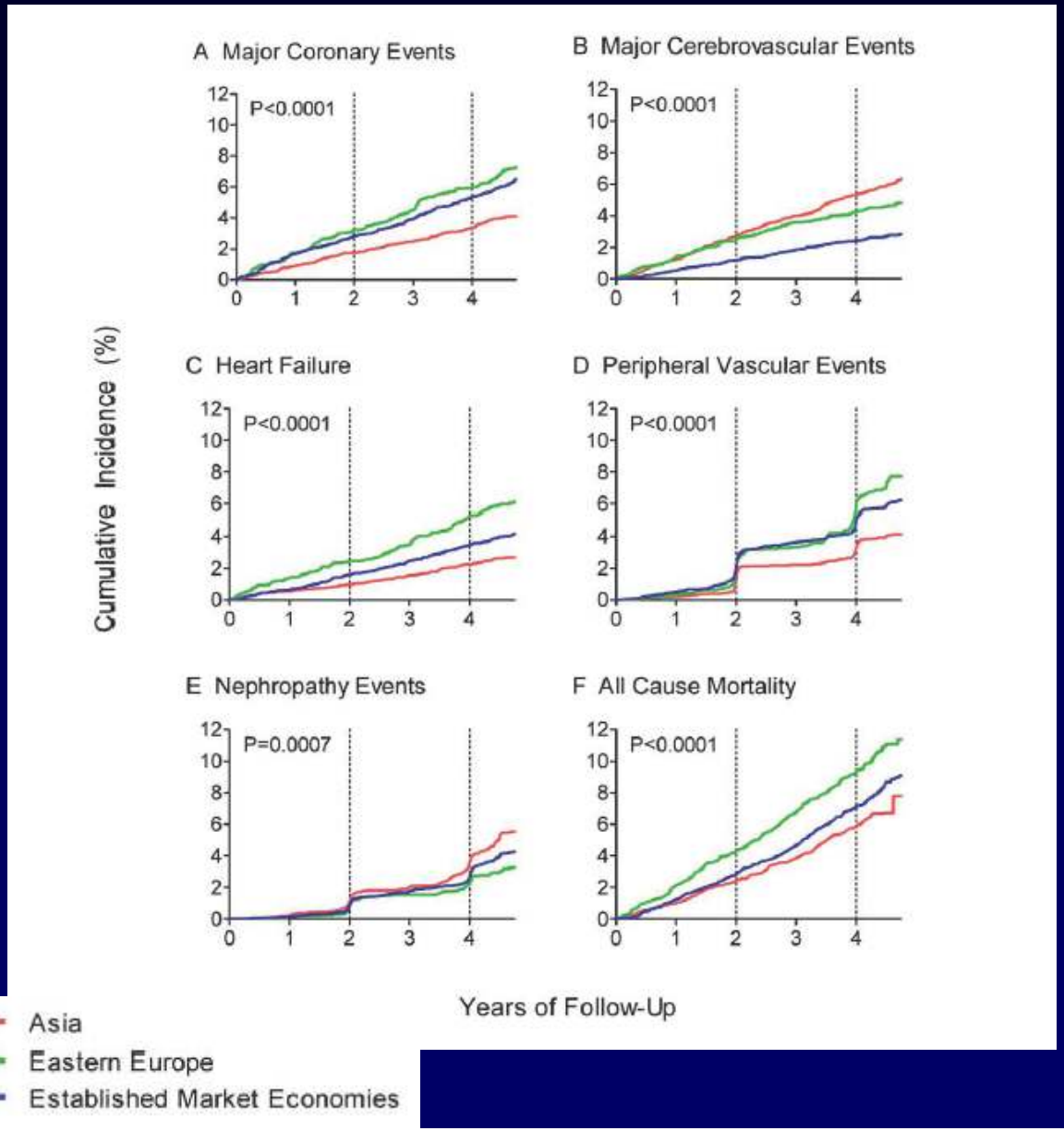
- MAPS study (Microalbuminuria Prevalence Study)
  - 6801 DM patients (50% Chinese) from 10 Asian countries
  - Macroalbuminuria 18.8%
  - Microalbuminuria 39.8%
  - Total 58.6%



Wu AP et al. Diabetologia 2005

Yoon et al, Lancet 2006; 368: 1681

Comparison of complications in Asians



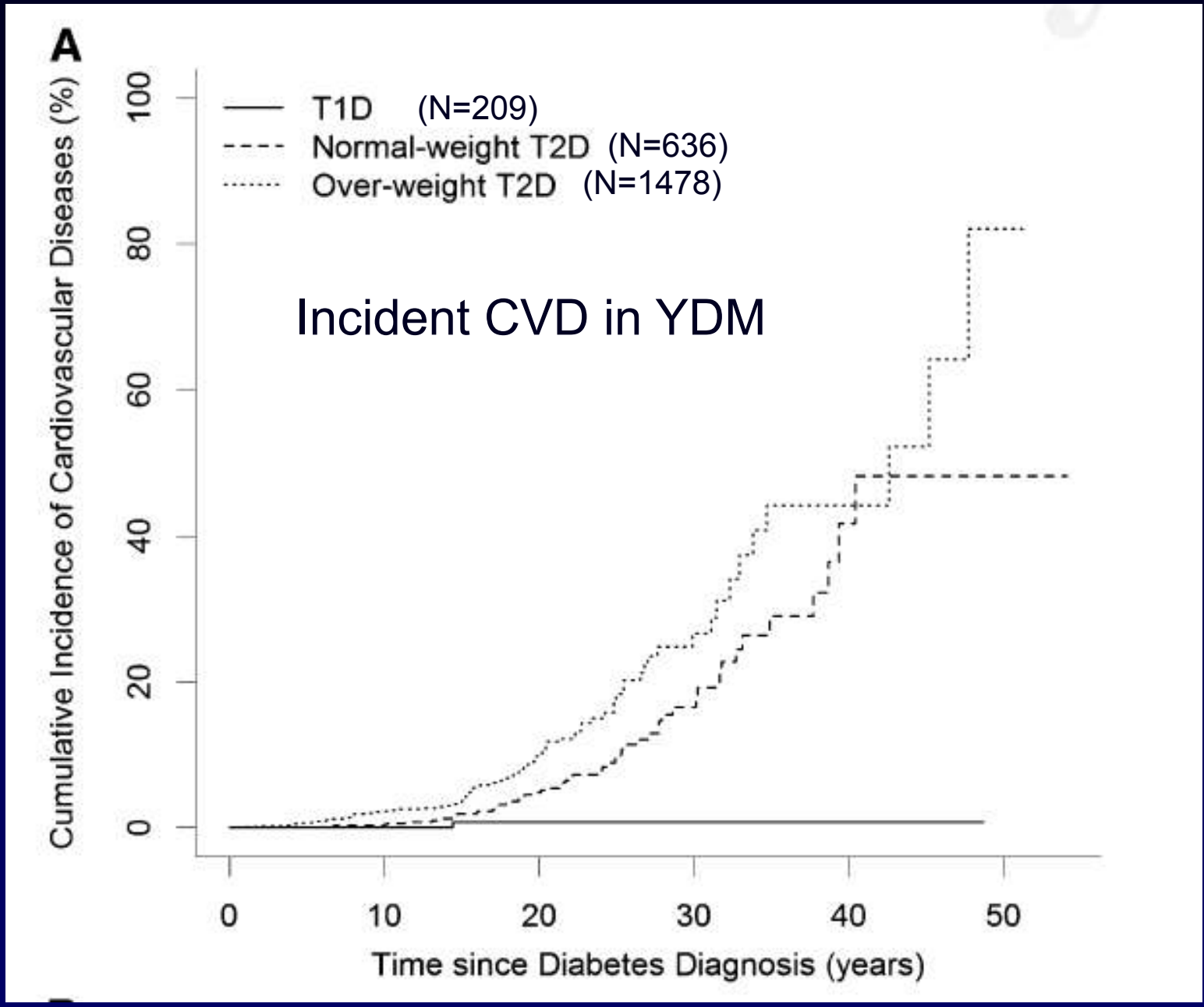
11140 T2 DM
ADVANCE study

Higher rate of renal Complications, Cerebrovascular cx

Clarke PM et al, PLoS Med 2010; Feb

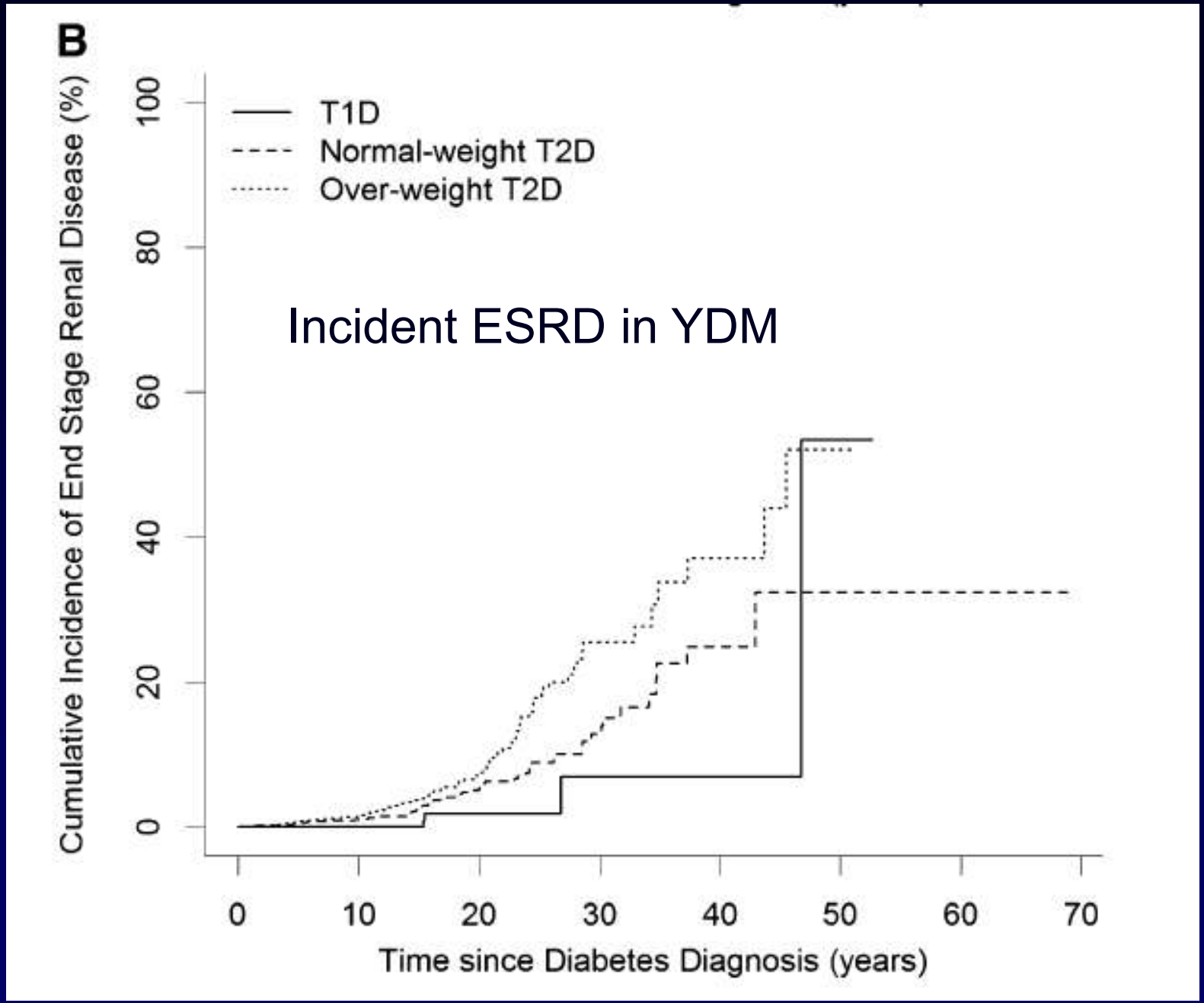
Parameter	UKPDS	ADVANCE	ACCORD	HKDR
Number pts	5,102	11,140	10,251	7,534
Follow-up (yrs)	10.0	5.0	3.5	6.0
Region	UK	Australia-NZ (13), Asia (37), Europe (46), N. Am (4)	North America	Hong Kong
Ethnicity	White (81), Indian Asian (10), black (8),	NR	White (64-65), black (19-20), hispanic (7-8)	Chinese (100)
Mean age (yrs)	53	62	66	56
Disease duration	0	8	10	5
Mean BMI (kg/m2)	28	28	32	25
Baseline HbA1c	7.1	7.2	8.1	7.5
Estimated annual incidence of outcome (%)				
All DM-rel. outcome	4.6	NR	NR	6.0
All-cause death	1.9	2.0	1.3	2.0
Cancer-related death	0.04	NR	0.04	0.08
Non-fatal MI	0.95	0.05	1.2	1.0
Non-fatal stroke	0.04	0.07	0.04	0.08
Heart failure	NR	0.08	0.06	0.08
Renal events	0.08	NR	NR	1.80

	Type 1 diabetes	Normal-weight type 2 diabetes	Overweight type 2 diabetes	*P*
n	209	636	1,478	
Age (years)	27.8 ± 11.5	41.9 ± 10.5	40.8 ± 9.5	<0.001
Male (%)	46.4	41.7	45.1	0.2850
Age at diabetes diagnosis (years)	19.5 ± 10.6	32.8 ± 6.2	33.0 ± 5.9	<0.0001
Time from diabetes diagnosis (years)	8 (2–12)	7 (1–14)	5 (1–12)	0.0060
Current or ex-smoker (%)	20.4	23.5	25.3	0.2553
Family history of diabetes (%)	22.0	54.1	59.7	<0.0001
BMI (kg/m^2)	21.7 ± 3.7	20.7 ± 1.8	27.8 ± 3.9	<0.0001
Waist circumference (cm)				
Male	76.0 ± 10.8	76.8 ± 5.9	92.9 ± 9.6	<0.0001
Female	70.8 ± 9.3	71.9 ± 6.2	86.9 ± 9.5	<0.0001
Systolic blood pressure (mmHg)	114.1 ± 15.1	120.3 ± 17.9	127.8 ± 17.2	<0.0001
HbA_{1c}				
NGSP (%)	8.6 ± 2.2	8.0 ± 2.2	7.8 ± 1.9	<0.0001
IFCC (mmol/mol)	66 ± 17	64 ± 18	62 ± 15	
LDL cholesterol (mmol/L)	2.8 ± 0.8	3.0 ± 1.0	3.1 ± 1.0	<0.0001
Triglyceride (mmol/L)	0.7 (0.5–1.0)	1.0 (0.7–1.4)	1.5 (1.1–2.4)	<0.0001
HDL cholesterol (mmol/L)	1.7 ± 0.5	1.5 ± 0.4	1.2 ± 0.3	<0.0001
Urine albumin-to-creatinine ratio (mg/mmol)	1.1 (0.6–2.3)	1.2 (0.6–3.6)	1.8 (0.7–8.8)	<0.0001
Estimated GFR (mL/min/1.73 m^2)	142.9 ± 42.6	126.7 ± 34.3	124.2 ± 36.4	<0.0001
Proportion with hypertension (%)	22.4	40.9	60.1	<0.0001
Proportion with dyslipidemia (%)	57.5	70.1	75.7	<0.0001
Baseline diabetes complications (%)				
Microalbuminuria	16.3	20.5	24.3	<0.0001
Macroalbuminuria	3.4	8.8	11.1	0.0050
Chronic kidney disease	0.5	3.1	4.9	0.0013
Retinopathy	14.8	23.3	22.9	0.0245
Peripheral neuropathy	10.5	17.9	15.4	0.0342
History of coronary heart disease	0.5	1.6	3.3	0.0069
History of stroke	0.0	0.6	0.9	0.4298
History of peripheral vascular disease	3.8	3.6	3.0	0.7105
Medication use at baseline (%)				
Insulin	100	22.0	19.0	<0.0001
Oral hypoglycemic drugs	4.8	45.9	59.0	<0.0001
Lipid-lowering drugs	1.9	6.6	12.4	<0.0001
Antihypertensive drugs	8.1	19.2	29.1	<0.0001



Median Follow-up period 9.3 years (6.2-11.6)

Luk AO et al, Diabetes Care, *in press*



Luk AO et al, Diabetes Care, *in press*

Increased risk of cardio-renal complications in obese T2DM vs T1DM

Model	Adj	HR	P
CVD			
Model 1	Age, gender, time from diagnosis	15.3 (2.08-112.4)	0.0073

Increased risk of cardio-renal complications in obese T2DM vs T1DM

Model	Adj	HR	P
CVD			
Model 1	Age, gender, time from diagnosis	15.3 (2.08-112.4)	0.0073
Model 2	Above + A1c	15.26 (2.07-112.3)	0.0075

Increased risk of cardio-renal complications in obese T2DM vs T1DM

Model	Adj	HR	P
CVD			
Model 1	Age, gender, time from diagnosis	15.3 (2.08-112.4)	0.0073
Model 2	Above + A1c	15.26 (2.07-112.3)	0.0075
Model 3	Above + BMI, SBP, DBP, LDL, TG, HDL	6.49 (0.83-50.7	0.074
Model 4	Above+eGFR, albuminuria, retinopathy, neuropathy	6.62 (0.84-52.)	0.074

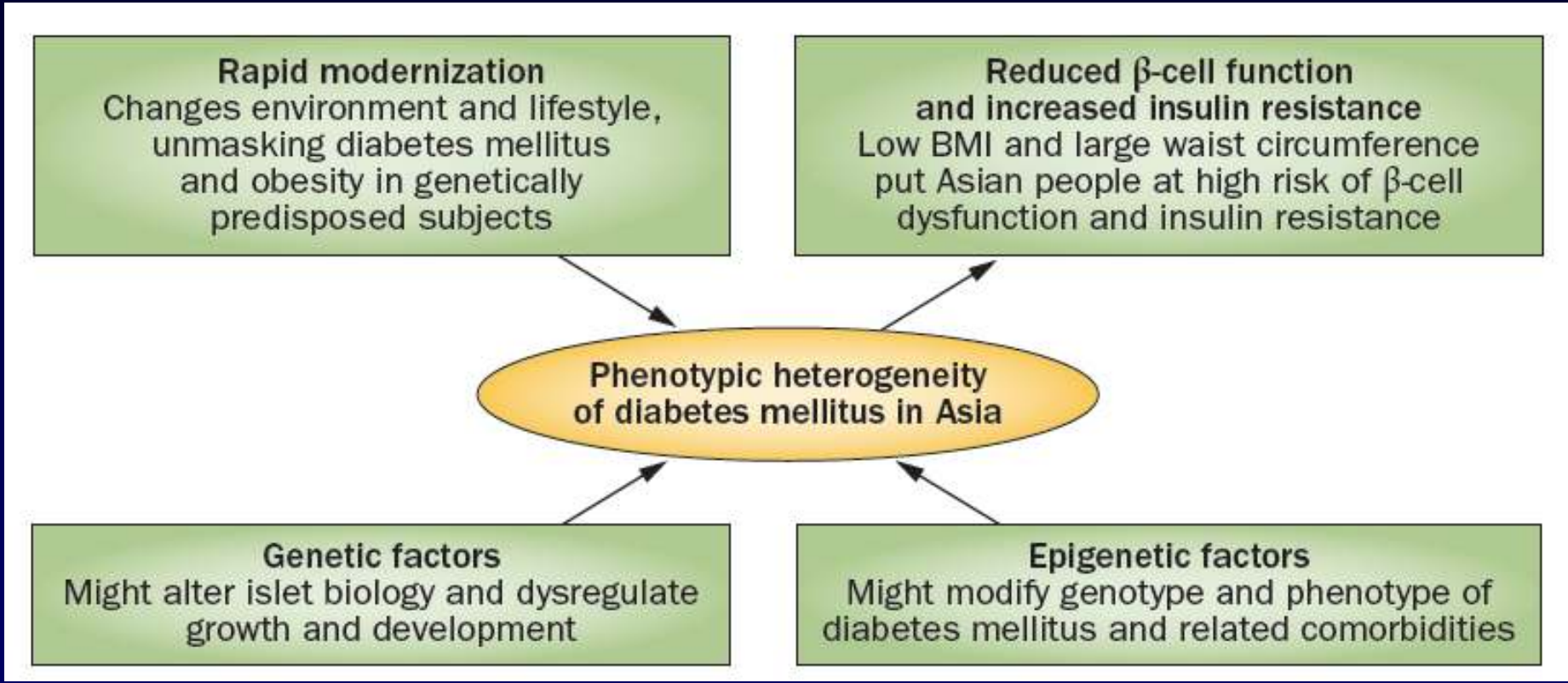
Model	Adj	HR	P
ESRD			
Model 1	Age, gender, time from diagnosis	5.41 (1.84-15.9)	0.0021
Model 2	Above + A1c	5.69 (1.69-16.8)	0.0017
Model 3	Above + BMI, SBP, DBP, LDL, TG, HDL	2.69 (0.69-10.5)	0.155
Model 4	Above+eGFR, albuminuria, retinopathy, neuropathy, hx CVD	2.35 (0.59-9.46)	0.228

No increased risk of cardio-renal complications in lean T2DM vs T1DM

Model	Adj	HR	P
CVD			
Model 1	Age, gender, time from diagnosis	6.03 (0.76-48.3)	0.091
Model 2	Above + A1c	6.43 (0.79-52.5)	0.082
Model 3	Above + BMI, SBP, DBP, LDL, TG, HDL	4.49 (0.47-43.4)	0.19
Model 4	Above+eGFR, albuminuria, retinopathy, neuropathy	3.7 (0.36-37.8)	0.27

Model	Adj	HR	P
ESRD			
Model 1	Age, gender, time from diagnosis	2.43 (0.76-7.8)	0.14
Model 2	Above + A1c	2.28 (0.71-7.28)	0.17
Model 3	Above + BMI, SBP, DBP, LDL, TG, HDL	2.03 (0.51-8.06)	0.32
Model 4	Above+eGFR, albuminuria, retinopathy, neuropathy, hx CVD	1.01 (0.23-4.46)	0.99

Phenotypic heterogeneity of Diabetes in Asians

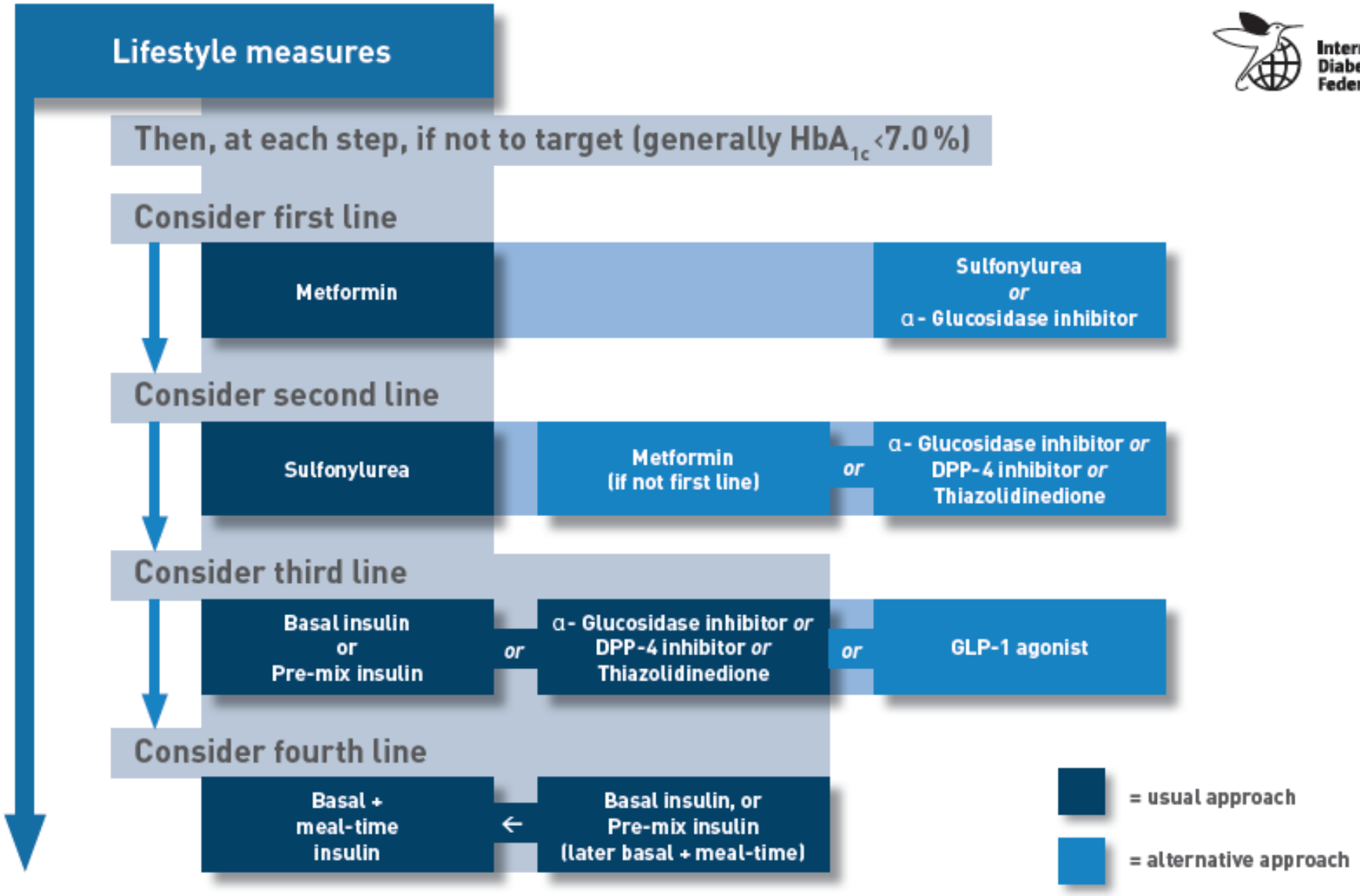


Kong AP, et al, Nat Rev Endocrinol 2013; May 28
Ma RC and Chan JC. Ann N Y Acad Sci 2013; April
Ramachandran A, Ma RC et al, Lancet 2010; 375: 408-18
Chan JC et al, JAMA 2009; May 27

Outline

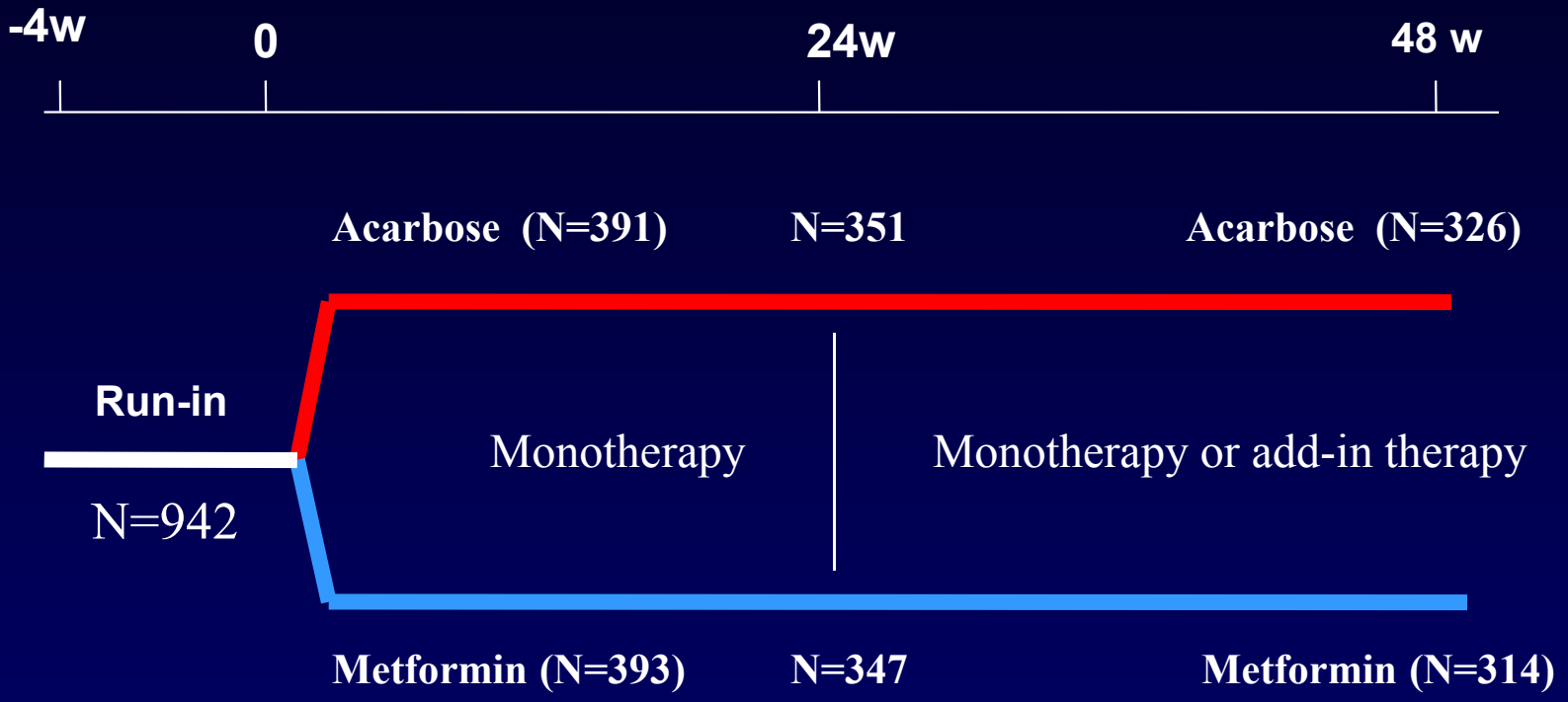
- Epidemiology of Diabetes in Asia
- Risk factors for DM in Chinese populations
- Familial young-onset DM
- Role of beta-cell dysfunction
- Genetic predictors of T2DM in E. Asians
- Role of visceral adiposity
- Increasing gestational diabetes
- Implications for treatment and prevention

IDF Treatment Algorithm for People with Type 2 Diabetes



International Diabetes Federation

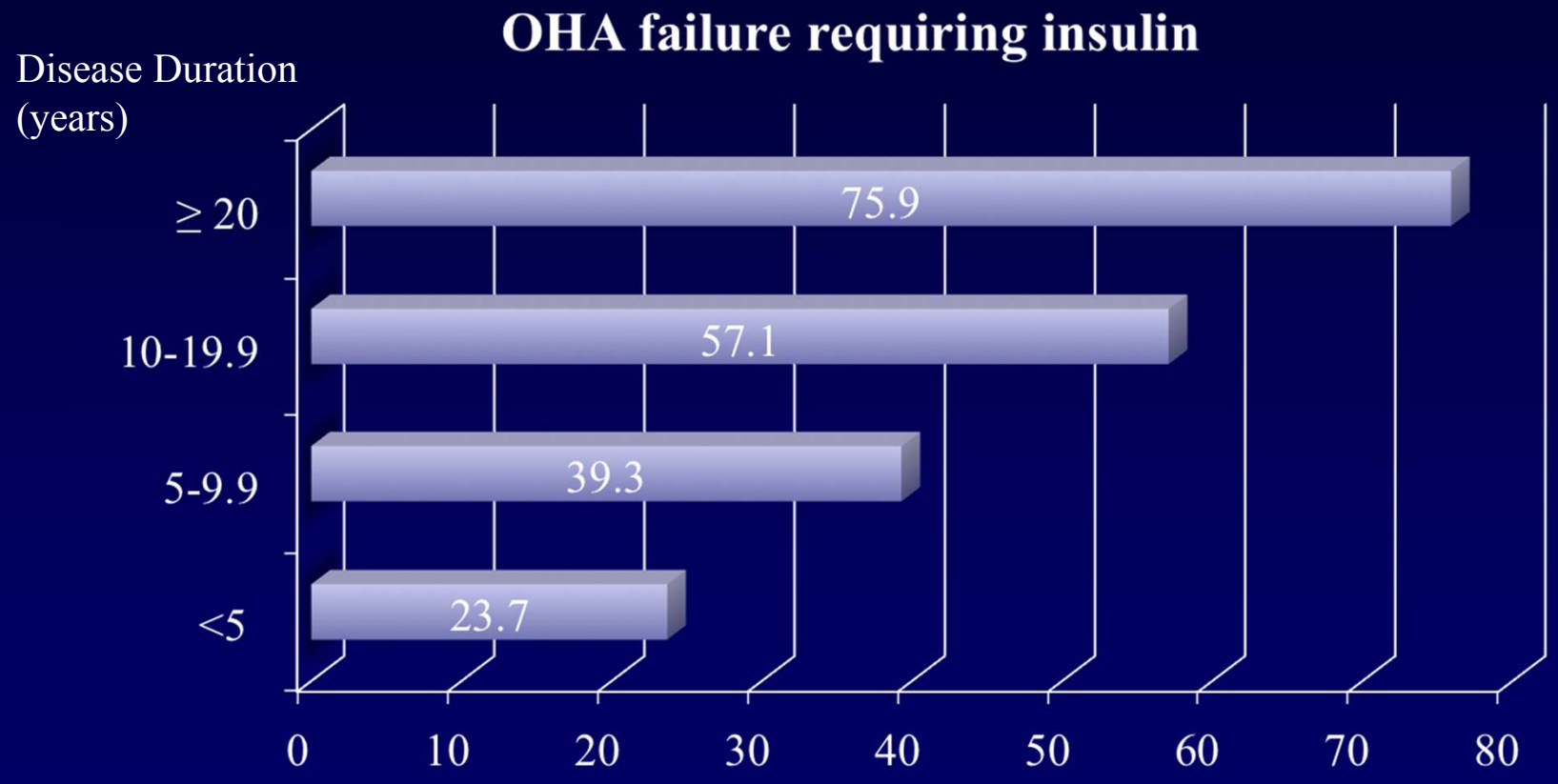
Metformin and AcaRbose in Chinese as the initial Hypoglyacemic treatment (MARCH) Trial



Mean HbA1c reduction at 48w: -1.11% acarbose vs -1.12% metformin
Acarbose group lost more weight: -0.63kg (-1.15 to -0.10, p=0.0194)
Acarbose group more favourable lipid profile
Acarbose less postprandial hyperinsulinaemia

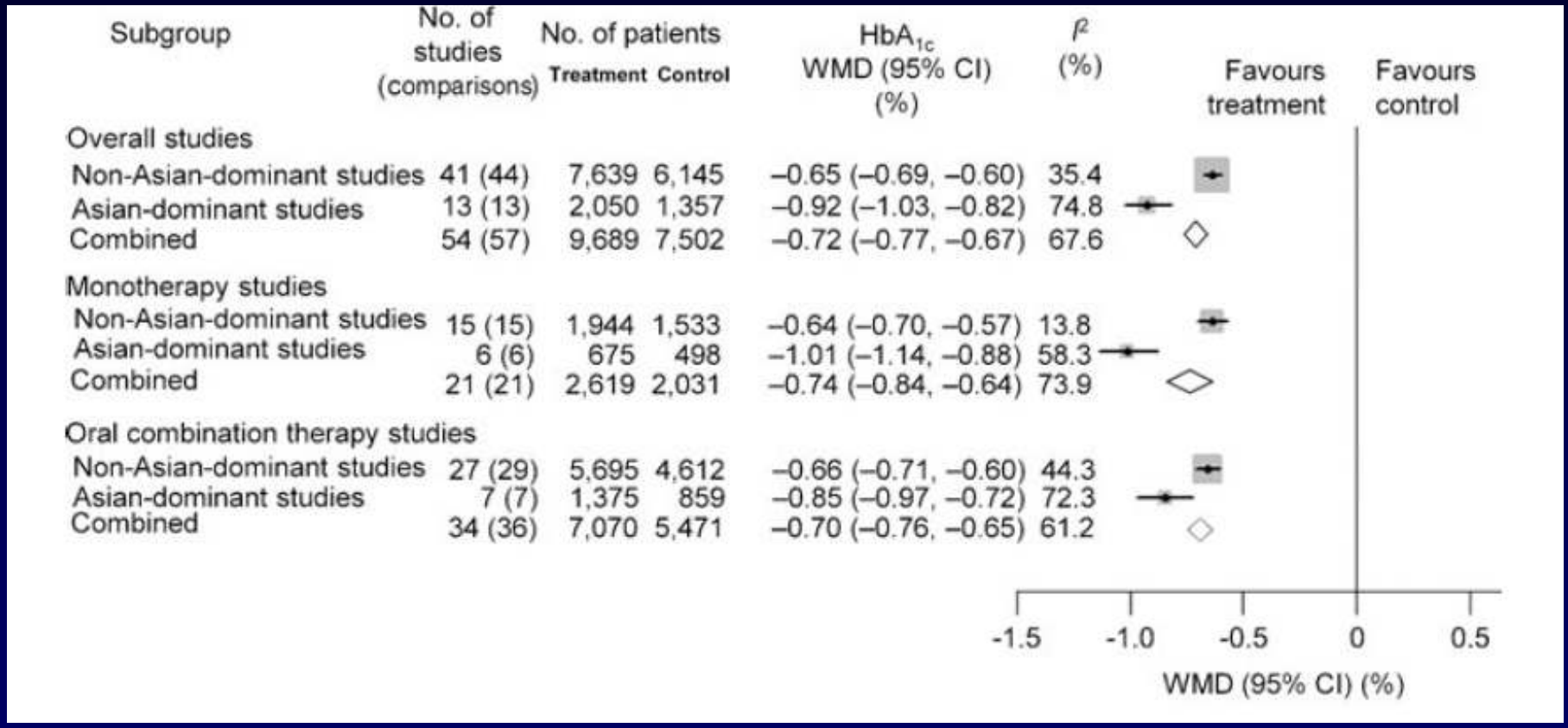
Yang W et al, Lancet Diabetes Endocrinol 2013; 18 Oct

OHA failure and need for insulin- Hong Kong Diabetes Registry



Tong PC et al, Diab Res Clin Pract 2008; 82: 346-352

Meta-analysis of 55 DPP4I trials comparing effect in Asians and Non-Asians



Combined difference in HbA1c -0.26%
Efficacy correlated with baseline BMI
Difference most marked for FBG

Kim YG et al, Diabetologia 2013; 56: 696-708

Feature	Eastern populations	Western populations
Subgroup with fastest increase in prevalence	Young and middle-aged individuals[6,8,146]	Elderly and migrant individuals[4,6,8]
Pattern of prediabetes	Predominantly impaired glucose tolerance, which is diagnosed using an oral glucose tolerance test[147]	Predominantly impaired fasting glycaemia Fasting plasma glucose level is the preferred test to diagnose diabetes mellitus[148]
Aetiology of early-onset diabetes (<35 years)	Considerable phenotypic and genetic heterogeneity Familial causes and obesity more important than autoimmunity[8]	Predominantly autoimmune etiology[149]
Principal driver of type 2 diabetes mellitus	Low BMI is common in populations with diabetes mellitus and reflects β-cell dysfunction[88,89]	High BMI is common in populations with diabetes mellitus and reflects insulin resistance[150]
Adiposity	Higher visceral fat for same BMI and waist circumference[151,152]	Lower visceral fat for same BMI[151,152]
Causes of insulin resistance	Pollutants, pathogen-rich environment (low-grade infections), and psychosocial stress Activation of innate inflammatory response exacerbates glucolipotoxicity[33,99,100,153–155]	Predominantly due to adiposity[156] Environmental factors and inflammation less important
Genetic factors	Autoimmune, mitochondrial and monogenic diabetes may account for 20% of cases of familial diabetes mellitus, especially in young patients with low lean body mass Few genomic studies have been conducted in Asian populations, suggesting many common variants are yet to be discovered[8,11,157–160]	Considerable interethnic differences in allelic locations and frequencies Common variants in white populations are rare in Asian individuals and vice versa
Epigenetic and perinatal programming	Low birth weight and maternal stress coupled with adolescent and childhood obesity suggest epigenetic phenomena are particularly relevant	Mismatching between biological and environmental factors potentially less important, except in migrant and indigenous populations
Complications	Stroke, renal disease and cancers that might have viral aetiologies Renal dysfunction is a main driver of cardiovascular disease[48]	Predominantly coronary heart disease[48]
Treatment responses	High use of sulfonylureas and α-glucosidase inhibitors High efficacy of dipeptidyl peptidase-4 inhibitors (reflecting differences in β-cell biology, dietary and cultural factors)[161,162]	Low α-glucosidase inhibitor use[60]
Health-care delivery	Less developed provision of integrated chronic care Major focus on treatment of acute and advanced diseases High use of traditional and complementary medicine Low levels of public awareness and patient education[122]	Developed health-care and coverage system, albeit with considerable social disparities in accessibility and affordability[163]

Kong AP, et al
Nat Rev
Endorinol
2013

Summary

- Escalating epidemic of type 2 DM in Asians
- Asians are at increased risk despite lower BMI
- Familial young-onset diabetes
- Important role of beta-cell dysfunction
- Role of visceral adiposity
- Increasing threat from Gestational Diabetes
- Strategies which target beta-cell dysfunction may be particularly relevant for Asian patients

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