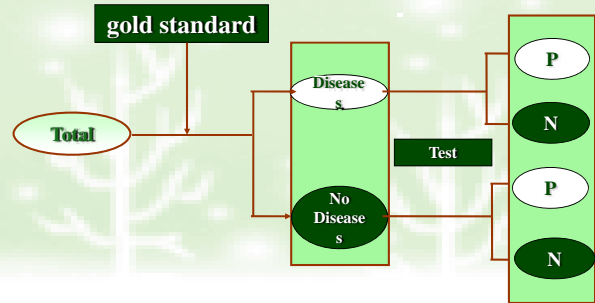


EBM~Journal Reading

張惠敏
970415

Diagnostic Procedure: Threshold Model

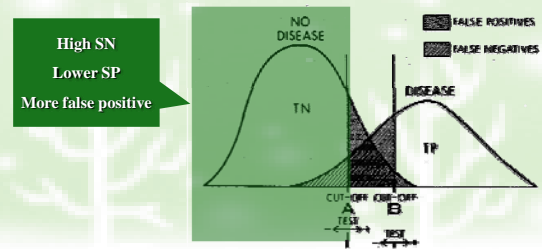


Test – Disease 2x2 set up table

	Disease (+)	Disease (-)	合計
Test (+)	真陽性(a)	假陽性(b)	a + b
Test (-)	假陰性(c)	真陰性(d)	c + d
合計	a + c	b + d	a + b + c + d

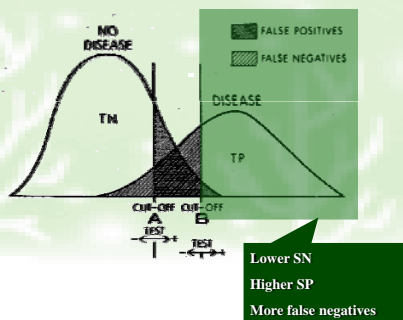
ROC Curve

Receive Operating Characteristic Curve(1)

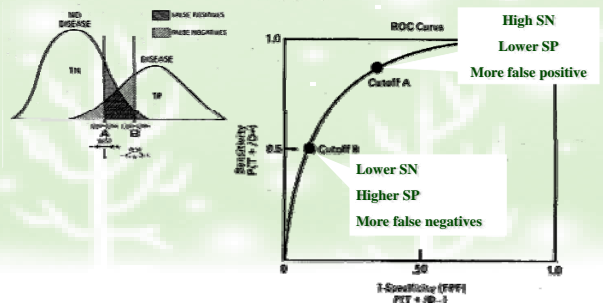


ROC Curve

Receive Operating Characteristic Curve(2)




ROC Curve : A Graphic Method for Comparing Two or More Diagnostic Tests



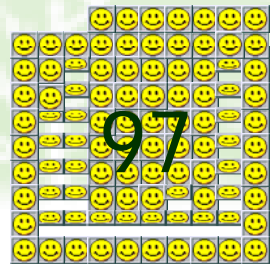
For a prevalence of 3% - in every 100 patients

3 will have the disease




Prevalence = (a+c)/(a+b+c+d)

	Disease (+)	Disease (-)	合计
Test (+)	真阳性	假阳性	a+b
Test (-)	假阴性	真阴性	c+d
合计	a+c (3)	b+d (97)	a+b+c+d (100)



97 Will not have the disease

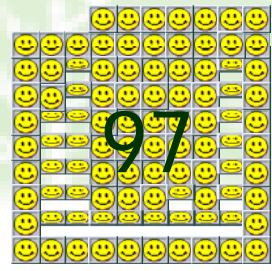
For a test with a sensitivity of 50%



For every 100 patients with the disease 1-2 will test positive


How many will not have the disease?

	Disease (+)	Disease (-)	合计
Test (+)	真阳性(1.5)	假阳性	a+b
Test (-)	假阴性(1.5)	真阴性	c+d
合计	a+c (3)	b+d (97)	a+b+c+d (100)



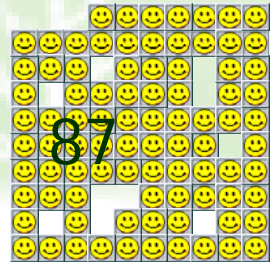
For a test with a specificity of 90%

	Disease (+)	Disease (-)	合计
Test (+)	真阳性(1.5)	假阳性(10)	a+b(11.5)
Test (-)	假阴性(1.5)	真阴性(87)	c+d(88.5)
合计	a+c (3)	b+d (97)	a+b+c+d (100)



False positive rate = 1-Specificity (10%)


For those who don't have the disease 10 patients will go on to test positive



87

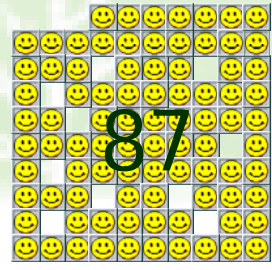
Given a positive test what are my chances of disease doc?

	Disease (+)	Disease (-)	合计
Test (+)	真阳性(1.5)	假阳性(10)	a+b(11.5)
Test (-)	假阴性(1.5)	真阴性(87)	c+d(88.5)
合计	a+c (3)	b+d (97)	a+b+c+d (100)



11 1/2 people have a positive test
Of which 1 1/2 will have the disease


13% chance of having the disease given a positive test



97

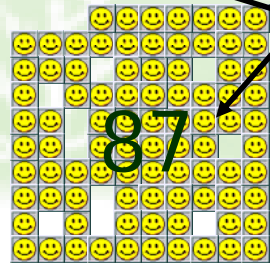
Given a negative test what are my chances of not having the disease doc?

	Disease (+)	Disease (-)	合计
Test (+)	真阳性(1.5)	假阳性(10)	a+b(11.5)
Test (-)	假阴性(1.5)	真阴性(87)	c+d(88.5)
合计	a+c (3)	b+d (97)	a+b+c+d (100)



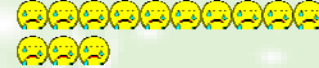
88 1/2 people will have a negative test of which 1 1/2 will have the disease

False reassurance rate of 1.7%



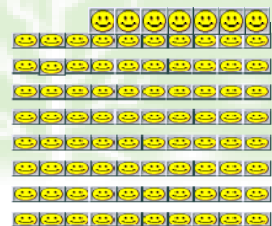
97

Describe the result to your patient



Positive predictive value

For every 100 people who have a positive test 13 will have the disease



What happens if I have an negative test



Negative test pretty much rules out the disease but a small number 1-2 people in every 100 will still have the disease

評價指標的計算

- 敏感度 = $a/(a+c)$
- 特異度 = $d/(b+d)$
- 陽性預測值 = $a/(a+b)$
- 陰性預測值 = $d/(b+d)$
- 診斷指數 = 敏感度 + 特異度
- 診斷效率(準確度) = $(a+d)/(a+b+c+d)$
- 陽性概似比 = 敏感度 / (1 - 特異度)
- 陰性概似比 = (1 - 敏感度) / 特異度

- 靈敏度(sensitivity)：真陽性率(真患者)試驗檢出已被gold standard確定為患者的能力 $a/(a+c)$
- 特異性(specificity)，真陰性率(非患者)試驗排除已被gold standard確定為非患者的能力 $d/(b+d)$
- 陽性預測值(positive predictive value) 陽性試驗的事後機率，某檢驗為陽性時被檢者患病的機率 $a/(a+b)$ 。
- 準確性(accuracy) 陰性試驗的事後機率，某檢驗為陰性時被檢者未患病的機率 $d/(c+d)$ 。

陽性試驗概似比

- 陽性試驗似然比(positive likelihood ratio, +LR) 患者試驗真陽性比例與非患者試驗假陽性比例的比值，表明試驗陽性時，患病與不患病機會的比值。比值越大(如 ≥ 10)，患病機率越大，試驗越好。
- $+LR = \text{靈敏度} / (1 - \text{特異性}) = [a/(a+c)] / [1 - d/(b+d)]$

陰性試驗似然比

- 陰性試驗似然比(negative likelihood ratio, -LR) 患者試驗假陰性比例與非患者試驗真陰性比例的比值，表明試驗陰性時，患病與不患病機會的比值。比值越小(如 ≤ 0.1)，不患病的機率越大，試驗越好。
- $-LR = (1 - \text{靈敏度}) / \text{特異性}$
- $= [1 - a/(a+c)] / [d/(b+d)]$

HbA1c as a screening tool for detection of Type 2 diabetes: a systematic review

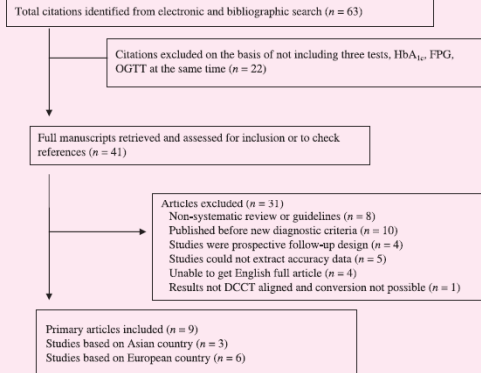
Diabet. Med. 24, 333–343 (2007)

Methods

- Databases: MEDLINE, PUBMED and EMBASE electron databases (1994–September 2004)
- Keywords: 'diabetes mellitus', 'screening', 'diagnosis', 'HbA1c', 'fasting plasma glucose test' and 'OGTT'.

Diabet. Med. 24, 333–343 (2007)

Criteria

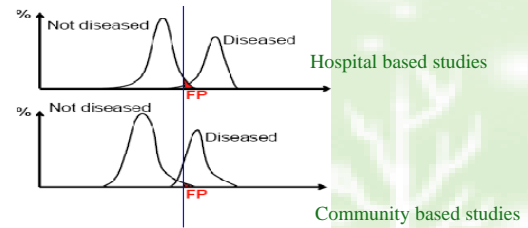


Diabet. Med. 24, 333–343 (2007)

First author, year and country	Settings	Recruitment methods	HbA _{1c} test method	Glucose method	Blood sample	Adequate test description	Verification with OGTT
Colagiuri 2004, Australia	Eighty-two randomly selected urban and non-urban areas (urban or vector districts)	≥ 25 years of age, household survey followed by household examination; 369 had 21 risk factor in accordance with Australian screening guideline	Roche affinity HPLC, normal range (3.6–4.7%), (V) not stated	Glucose oxidase	Venous plasma	Good	100%
Mannucci 2005, Italy	A suburban community of the southern of Florence	50–70-year-old self-referred general population	HPLC (HAI121, Menarini) Diagnostic upper limit 5.7% (V) not stated	Glucose oxidase	Venous plasma	Adequate	100%
Serdan 2002, USA	National Center for Health (NHANES II) participants	Age 40–74, BMI < 24 kg/m ² with IGT	Roche glucose HPLC (Bio-Rad) Laboratories CV 2%, normal range 4.1–6.1%	Hexokinase	Venous plasma	Poor	100%
Wynn 1998, UK	Two sites in the UK	GI referred high risk of DM 13–92 years	Roche glucose HPLC (Daiki) HAI100RLH, CV2% Normal range: (3.3–5.3%)	Hexokinase	Capillary plasma	Adequate	100%
Hendrik 2003, Poland	Endocrine Test Unit at the Dept of Adult Hospital	Volunteers with high risks of DM (obesity, family history of diabetes and gestational diabetes, symptoms of polyuria and polydipsia) ≥ 18 years of age, suspicion of having diabetes as a result of symptoms or having known risk factors for IGT	HPLC (Pharmacia HPLC System) CV (0.47–0.94%) Normal range: 3.8–5.2%	Hexokinase	Venous plasma	Good	100%
Tanaka 2001, Japan	Academy of Medicine-Saitama Central Hospital and Juntendo University Hospital Tokyo	Suspected of having DM, excluded anemia (Hb < 12 g/dl) and renal for hepatic dysfunction	HPLC (V23GMB III, Toho Corp.) Normal range: 4.3–5.8%	Not stated	Venous plasma	Poor	100%
Tanisharan 2000, Singapore	Volunteers attending the hospital (long proposition were more)	< 55 years of age, family history, hypertension, hyperlipidemia, with BMI > 24 kg/m ² , creatinine renal liver, or cardiac disease and previous gastroscopy	DCA 2000 (CV 3.3%) Normal range: 4.2–6.5%	Spectro analyzer	Venous plasma	Adequate	100%
Lo 1998, Hong Kong	Diabetes and Endocrine Center of Wai Kwo Hospital for diabetes screening	High risk for IGT family history of diabetes, gestational diabetes, history of IGT and obesity	Automated ion-exchange chromatographic method (Bio-Rad) Laboratories, CV = 3.1% normal range: 3.1–6.4%	Oxidase	Venous plasma	Adequate	100%

Diabet. Med. 24, 333–343 (2007)

Effects of patient spectrum: Specificity



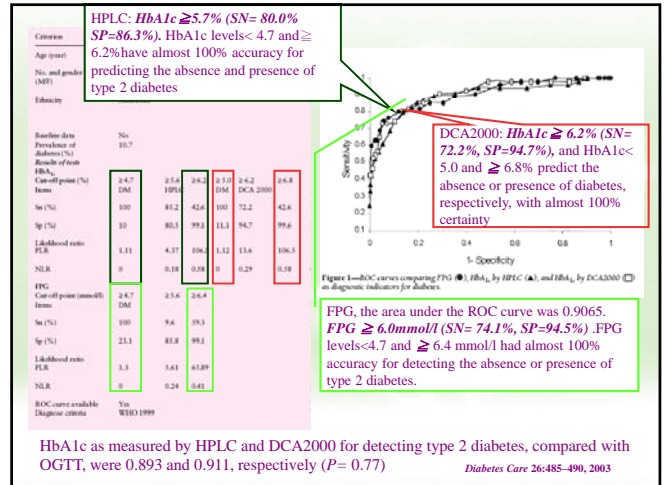
Criterion	Colagiuri et al.	Mannucci et al.*	Serdan et al.	Wynn and Roberts*
Age (year)	> 25 years summary statistics not reported	52.2 ± 18.5 (50–70)	40–74	13–92
No. and gender (M/F)	10/447	1215	2844	401
Ethnicity	Australia national population	Italian	USA	2089/953
Baseline data	No	Yes	No	No
Prevalence of diabetes (%)	7.4	6.6	6.2 (ADA criteria)	4.4
Results of tests				
HbA _{1c}				
Cut-off point (%)	2.3.3	> 6.6	2.5.5 2.6.0	> 6.9 > 7.4 > 7.6
Items	DM4 IGT	DM4 IGT	IGT	DM4
Se (%)	78.7 42.0	M 78 M 59	60.0 16.7	64.0 50.6 41.0
Sp (%)	82.8 88.2	M 30 M 19	55.0 92.9	91.0 98.2 100
Sp (%)	F 21 F 9	F 108 F 85	F 108 F 85	F 21 F 9
Likelihood ratio				
PLR	4.58 3.56	M 1.30 M 0.75	1.33 2.35	7.11 28.11 =
NLR	0.26 0.66	F 1.28 F 0.60	0.73 0.90	0.40 0.50 0.59
FFG				
Cut-off point (mmol/l)	> 5.5 > 6.1	> 7.0 > 6.1	> 5.6 > 6.1	> 6.0 > 6.9
Items	DM4 IGT	DM4 IGT	DM4 IGT	DM4 IGT
Se (%)	79.9 63.6	M 91 M 59	76.5 34.9	89.9 78.1
Sp (%)	51.9 34.6	M 30.0 M 19.3	37.9 86.9	65.9 87.9
Sp (%)	79.9 93.9	F 21.6 F 9.3	F 21.6 F 9.3	F 21.6 F 9.3
Likelihood ratio				
PLR	3.98 10.4	L 30 0.73	1.23 2.66	2.64 6.45
NLR	3.9 =	L 28 0.60		
NLR	0.25 0.39	0.31 2.12		
NLR	0.55 0.65	0 4.86		
ROC curve available	No	Yes (for IGT)	Yes	Yes
Diagnose criteria	WHO (1999)	WHO (1999)	WHO (1999)	WHO 28 OGTT

Diabet. Med. 24, 333–343 (2007)

Criterion	Jendryaszek et al.	Hendrik et al.*	Tanaka et al.	Tanisharan et al.	Lo et al.
Age (year)	53.8 (19–88)	> 18 (18–82)	36	43.2 (15–50)	Mean 53
No. and gender (M/F)	501	128/105	866	111	2877
Ethnicity	Australian	Polish	Japanese	Chinese Indian Malays Others	1816/504/474/111
Baseline data	No	Yes	No	No	Yes
Prevalence of diabetes (%)	10.7	19	20.6	17	21
Results of tests					
HbA _{1c}					
Cut-off point (%)	2.4.7	2.4.4	2.4.4	2.7.0	2.4.0 2.3.8
Items	DM4 IGT	DM4 IGT	DM4 IGT	DM4 IGT	DM4 IGT
Se (%)	100	81.2 42.6 100 72.2 42.6	73.7 31.3 76 49	95 32 81 81 48	77.5 80.2 91.7 88.4 84.4
Sp (%)	10	80.3 99.1 11.1 94.7 99.6	93.2 95.8 86 98	67 97 84 88 96	78.8 84.6 88.8 84.4 84.4
Likelihood ratio					
PLR	1.11	4.37 196.3 1.32 13.4 196.3	10.84 12.2 1.43 24.3	2.88 17.3 3.06 4.73 2.8	3.66 1.63 1.37 1.37 1.37
NLR	0	0.18 0.58 0 0.29 0.58	0.28 0.31 0.28 0.52	0.07 0.49 0.23 0.22 0.33	0.29 0.89 0.41
FFG					
Cut-off point (mmol/l)	2.4.7	2.4.4	2.4.4	2.7.0	2.4.0 2.3.8
Items	DM4 IGT	DM4 IGT	DM4 IGT	DM4 IGT	DM4 IGT
Se (%)	100	9.6 39.3	77.7 42.6 32	19 48 32 52	83.3 88.4 84.4 84.4 84.4
Sp (%)	23.1	81.8 99.1	100 100 100	100 98 98 90	84.4 79.2 87.7 84.4 84.4
Likelihood ratio					
PLR	1.3	3.63 65.89	= = =	2.4 2.4 1.2	3.86 4.23 1.24 1.24 1.24
NLR	0	0.24 0.41	0.33 0.33 0.33	0.49 0.49 0.33 0.33	0.18 0.13 0.41 0.41 0.41
ROC curve available	Yes	Yes	No	Yes	No
Diagnose criteria	WHO 1999	WHO 1999	WHO 28 OGTT	WHO 28 OGTT and ADA (1997)	WHO 28 OGTT

Macrovascular Risk and Diagnostic Criteria for Type 2 Diabetes

Diabetes Care 26:485–490, 2003



Fasting plasma glucose and HbA1c to predict diabetes

Diabetes care, volume 21, number 8, august 1998

Fasting plasma glucose and HbA1c to predict diabetes

- N=2,877 Hong Kong Chinese subjects
- These subjects had known risk factors for glucose intolerance and were referred to the Diabetes and Endocrine Center of the Prince of Wales Hospital for diabetes screening.
 - The risk factors for glucose intolerance included a family history of diabetes
 - history of gestational diabetes
 - Obesity
 - history of impaired glucose tolerance.

DIABETES CARE, VOLUME 21, NUMBER 8, AUGUST 1998

Fasting plasma glucose and HbA1c to predict diabetes

- The test was performed after 3 days of normal carbohydrate intake and physical activity and after an 8-h fast.
- No smoking was allowed during the test.
- FPG and 2-h PG were measured together with HbA1c and fructosamine.
- Both the WHO and ADA criteria were used for the diagnosis of glucose intolerance

DIABETES CARE, VOLUME 21, NUMBER 8, AUGUST 1998

Fasting plasma glucose and HbA1c to predict diabetes

FPG (mmol/l)	HbA _{1c} (%)	Number of subjects	75-g OGTT		
			Normal	IGT	Diabetes
≥ 5.6	≥ 5.5	880	132	221	527
≥ 5.6	< 5.5	143	64	52	27
< 5.6	≥ 5.5	965	683	234	48
< 5.6	< 5.5	889	714	150	25
		Total	2,877	1,593 (55.4%)	627 (21.8%)

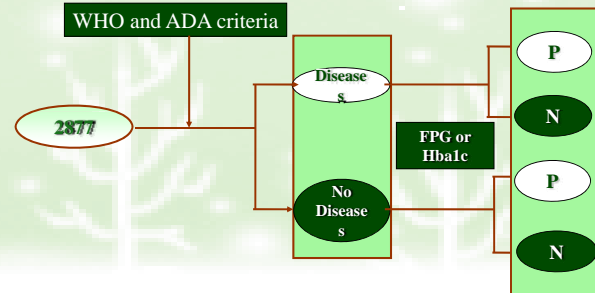
DIABETES CARE, VOLUME 21, NUMBER 8, AUGUST 1998

Fasting plasma glucose and HbA1c to predict diabetes

FPG (mmol/l)	Fructosamine (μmol/l)	Number of subjects	75-g OGTT		
			Normal	IGT	Diabetes
≥5.4	≥235	695	154	164	377
≥5.4	<235	254	142	69	43
<5.4	≥235	684	546	102	36
<5.4	<235	775	660	108	7
Total		2,408	1,502 (62.4%)	443 (18.4%)	463 (19.2%)

DIABETES CARE, VOLUME 21, NUMBER 8, AUGUST 1998

Fasting plasma glucose and HbA1c to predict diabetes



Fasting plasma glucose and HbA1c to predict diabetes

FPG (mmol/l)	HbA1c (%)	Number of subjects	75-g OGTT		
			Normal	IGT	Diabetes
≥5.6	≥5.5	880	132	221	527
≥5.6	<5.5	143	64	52	27
<5.6	≥5.5	965	683	234	48
<5.6	<5.5	889	714	150	25
Total		2,877	1,593 (55.4%)	657 (22.8%)	627 (21.8%)

	D(+)	D	D(-)
Test (+)	575	1270	980
Test (-)	52	980	575

$527+48=575$
 $132+221+683+234=1270$
 $27+25=52$
 $64+52+714+150=980$

DIABETES CARE, VOLUME 21, NUMBER 8, AUGUST 1998

Fasting plasma glucose and HbA1c to predict diabetes

FPG (mmol/l)	HbA1c (%)	Number of subjects	75-g OGTT		
			Normal	IGT	Diabetes
≥5.6	≥5.5	880	132	221	527
≥5.6	<5.5	143	64	52	27
<5.6	≥5.5	965	683	234	48
<5.6	<5.5	889	714	150	25
Total		2,877	1,593 (55.4%)	657 (22.8%)	627 (21.8%)

	D(+)	D(-)
Test (+)	575	1270
Test (-)	52	980

DM

$$SN(\%) = 575 / (575 + 52) \times 100\% = 91.7\%$$

$$SP(\%) = 980 / (1270 + 980) \times 100\% = 43.6\%$$

$$PLR = 0.917 / (1 - 0.436) = 1.63$$

DIABETES CARE, VOLUME 21, NUMBER 8, AUGUST 1998

$$NLR = (1 - 0.917) / 0.436 = 0.19$$

Fasting plasma glucose and HbA1c to predict diabetes

FPG (mmol/l)	HbA1c (%)	Number of subjects	75-g OGTT		
			Normal	IGT	Diabetes
≥5.6	≥5.5	880	132	221	527
≥5.6	<5.5	143	64	52	27
<5.6	≥5.5	965	683	234	48
<5.6	<5.5	889	714	150	25
Total		2,877	1,593 (55.4%)	657 (22.8%)	627 (21.8%)

	D(+)	D	D(-)
Test (+)	1030	815	778
Test (-)	254	778	1030

$221+234+527+48=1030$
 $52+150+27+25=254$
 $132+683=815$
 $64+714=778$

DIABETES CARE, VOLUME 21, NUMBER 8, AUGUST 1998

Fasting plasma glucose and HbA1c to predict diabetes

FPG (mmol/l)	HbA1c (%)	Number of subjects	75-g OGTT		
			Normal	IGT	Diabetes
≥5.6	≥5.5	880	132	221	527
≥5.6	<5.5	143	64	52	27
<5.6	≥5.5	965	683	234	48
<5.6	<5.5	889	714	150	25
Total		2,877	1,593 (55.4%)	657 (22.8%)	627 (21.8%)

	D(+)	D(-)
Test (+)	1030	815
Test (-)	254	778

IGT

$$SN(\%) = 1030 / (1030 + 254) \times 100\% = 80.2\%$$

$$SP(\%) = 778 / (815 + 778) \times 100\% = 48.8\%$$

$$PLR = 0.802 / (1 - 0.488) = 1.57$$

DIABETES CARE, VOLUME 21, NUMBER 8, AUGUST 1998

$$NLR = (1 - 0.802) / 0.488 = 0.41$$

Fasting plasma glucose and HbA1c to predict diabetes

FPG (mmol/l)	HbA1c (%)	Number of subjects	75-g OGTT		
			Normal	IGT	Diabetes
≥5.6	≥5.5	880	132	221	527
≥5.6	<5.5	143	64	52	27
<5.6	≥5.5	965	683	234	48
<5.6	<5.5	889	714	150	25
Total		2,877	1,593 (55.4%)	657 (22.8%)	627 (21.8%)

	D(+)	D(-)
Test (+)	554 $527+27=554$	469 $132+221+64+52=469$
Test (-)	73 $48+25=73$	1781 $683+234+714+150=1781$

DIABETES CARE, VOLUME 21, NUMBER 8, AUGUST 1998

Fasting plasma glucose and HbA1c to predict diabetes

FPG (mmol/l)	HbA1c (%)	Number of subjects	75-g OGTT		
			Normal	IGT	Diabetes
≥5.6	≥5.5	880	132	221	527
≥5.6	<5.5	143	64	52	27
<5.6	≥5.5	965	683	234	48
<5.6	<5.5	889	714	150	25
Total		2,877	1,593 (55.4%)	657 (22.8%)	627 (21.8%)

	D(+)	D(-)
Test (+)	554	469
Test (-)	73	1781

DM
 $SN(\%) = 554 / (554 + 73) \times 100\% = 88.4\%$
 $SP(\%) = 1781 / (469 + 1781) \times 100\% = 79.2\%$
 $PLR = 0.884 / (1 - 0.792) = 4.25$
 $NLR = (1 - 0.884) / 0.792 = 0.15$

DIABETES CARE, VOLUME 21, NUMBER 8, AUGUST 1998

Fasting plasma glucose and HbA1c to predict diabetes

FPG (mmol/l)	HbA1c (%)	Number of subjects	75-g OGTT			Likelihood ratio	
			Normal	IGT	Diabetes	Abnormal	Diabetes
≥5.6	≥5.5	880	132	221	527	7.03	5.36
≥5.6	<5.5	143	64	52	27	1.53	0.84
<5.6	≥5.5	965	683	234	48	0.51	0.19
<5.6	<5.5	889	714	150	25	0.30	0.10
Total		2,877	1,593 (55.4%)	657 (22.8%)	627 (21.8%)		

	D(+)	D(-)
Test (+)	827 $221+52+527+27=827$	196 $132+64=196$
Test (-)	457 $234+150+48+25=457$	1397 $683+714=1397$

DIABETES CARE, VOLUME 21, NUMBER 8, AUGUST 1998

Fasting plasma glucose and HbA1c to predict diabetes

FPG (mmol/l)	HbA1c (%)	Number of subjects	75-g OGTT		
			Normal	IGT	Diabetes
≥5.6	≥5.5	880	132	221	527
≥5.6	<5.5	143	64	52	27
<5.6	≥5.5	965	683	234	48
<5.6	<5.5	889	714	150	25
Total		2,877	1,593 (55.4%)	657 (22.8%)	627 (21.8%)

	D(+)	D(-)
Test (+)	827	196
Test (-)	457	1397

IGT
 $SN(\%) = 827 / (827 + 457) \times 100\% = 64.4\%$
 $SP(\%) = 1397 / (196 + 1397) \times 100\% = 87.7\%$
 $PLR = 0.644 / (1 - 0.877) = 5.24$
 $NLR = (1 - 0.644) / 0.877 = 0.41$

DIABETES CARE, VOLUME 21, NUMBER 8, AUGUST 1998

Criterion	Colagiuri et al.
Age (year)	> 25 years summary statistics not reported
No. and gender (M/F)	10,447
Ethnicity	Not stated
Baseline data	Australia national population
Prevalence of diabetes (%)	No
Results of tests	7.4
HbA1c	
Cut-off point (%)	≥ 5.2
Items	DM IGT
Sn (%)	78.7 42.0
Sp (%)	82.8 88.2
Likelihood ratio	
PLR	4.58 3.56
NLR	0.26 0.66
FPG	
Cut-off point (mmol/l)	≥ 5.5 ≥ 6.1
Items	DM IGT
Sn (%)	79.9 63.6
Sp (%)	51.9 34.6
Likelihood ratio	
PLR	3.98 10.4
NLR	3.9 0.39
NLR	0.55 0.65
B.O.C. curve available	No
Diagnose criteria	WHO (1999)

IGT: HBA1C had a lower sensitivity, but higher specificity

IGT: FPG had a lower sensitivity

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Criterion	Mansueti et al*
Age (year)	52.2 ± 18.5 (80-70)
No. and gender (M/F)	2119
Ethnicity	Italian
Baseline data	Yes
Prevalence of diabetes (%)	6.6
Results of tests	
HbA1c	
Cut-off point (%)	> 6.6
Items	DM IGT
Sn (%)	M 96 M 59
Sp (%)	F 100 F 55
Likelihood ratio	
PLR	M 1.36 M 0.73
NLR	F 1.28 F 0.40
FPG	
Cut-off point (mmol/l)	≥ 7.0 ≥ 6.1
Items	DM IGT
Sn (%)	M 91 M 59
Sp (%)	M 90 M 55
Likelihood ratio	
PLR	1.30 3.73
NLR	1.28 3.60
NLR	0.31 2.12
NLR	0 4.86
B.O.C. curve available	Yes (for IGT)
Diagnose criteria	WHO 1999

IGT: HBA1C had a lower sensitivity and specificity

Diabet. Med. 24, 333-343 (2007)

Criterion	Colagueri et al.	Mammucci et al.*	Seydan et al.	Wener and Roberts*
Age (year)	> 25 years summary statistics not reported	52.2 ± 18.5 (30-70)	40-74	13-92
No. and gender (M/F)	10 447	1215	2844	401
Ethnicity	Not stated	5676/48 Italian	Not stated USA	209/193 UK
Baseline data	No	Yes	No	No
Prevalence of diabetes (%)	7.4	6.6	6.2 (ADA criteria)	4.4
Results of tests				
HbA _{1c}				
Cut-off point (%)	≥ 5.1	≥ 6.6	≥ 5.5 > 6.0	≥ 6.9 > 7.4 > 7.6
Items			IGT	DM
Se (%)	99	99	60.0 16.7	64.0 50.6 41.0
Sp (%)	99	99	87.0 92.9	91.0 98.2 100
Likelihood ratio				
PLR	379	379	1.33 2.35	7.11 26.11 --
NLR	0.26 0.66	M 0.31 F 0.60 M 2.12 F 4.86	0.73 0.90	0.40 0.50 0.59
FPG				
Cut-off point (mmol/l)	2.5-5 2.6-1	7.0 7.6	2.5-6 2.6-1	≥ 6.0 ≥ 6.7
Items	DM DM	DM KGT	IGT	DM
Se (%)	79.9 63.6	M 91 M 19	76.5 34.9	89.9 78.1
Sp (%)	79.9 93.9	M 30.0 M 19.3 F 21.6 F 9.3	87.9 86.9	65.9 87.9
Likelihood ratio				
PLR	3.98 10.4	1.30 3.73	1.23 2.65	2.64 6.45
NLR	0.25 0.59	0.31 2.12		
ROC curve available	No	Yes (for KGT)	Yes	Yes
Diagnose criteria	WHO (1999)	WHO (1999)	WHO (1999)	WHO 24 OGTT

HbA1c had a lower sensitivity, but higher specificity

higher specificity of HbA1c

higher sensitivity of FPG

Criterion	Colagueri et al.	Mammucci et al.*	Seydan et al.	Wener and Roberts*
Age (year)	> 25 years summary statistics not reported	52.2 ± 18.5 (30-70)	40-74	13-92
No. and gender (M/F)	10 447	1215	2844	401
Ethnicity	Not stated	5676/48 Italian	Not stated USA	209/193 UK
Baseline data	No	Yes	No	No
Prevalence of diabetes (%)	7.4	6.6	6.2 (ADA criteria)	4.4
Results of tests				
HbA _{1c}				
Cut-off point (%)	≥ 5.1	≥ 6.6	≥ 5.5 > 6.0	≥ 6.9 > 7.4 > 7.6
Items	IGT DM	IGT DM	IGT DM	DM
Se (%)	78.7 82.8	M 98 M 29	60.0 16.7	64.0 50.6 41.0
Sp (%)	82.8		87.0 92.9	91.0 98.2 100
Likelihood ratio				
PLR	4.58 3.56	M 1.30 M 0.73	1.33 2.35	7.11 26.11 --
NLR	0.26 0.66	M 0.31 M 2.12 F 0 F 4.86	0.73 0.90	0.40 0.50 0.59
FPG				
Cut-off point (mmol/l)	2.5-5 2.6-1	7.0 7.6	2.5-6 2.6-1	≥ 6.0 ≥ 6.7
Items	DM DM	DM KGT	IGT	DM
Se (%)	79.9 63.6	M 91 M 19	76.5 34.9	89.9 78.1
Sp (%)	79.9 93.9	M 30.0 M 19.3 F 21.6 F 9.3	87.9 86.9	65.9 87.9
Likelihood ratio				
PLR	3.98 10.4	1.30 3.73	1.23 2.65	2.64 6.45
NLR	0.25 0.59	0.31 2.12		
ROC curve available	No	Yes (for KGT)	Yes	Yes
Diagnose criteria	WHO (1999)	WHO (1999)	WHO (1999)	WHO 24 OGTT

Criterion	Jendryas et al.	Hedvik et al.*	Tanaka et al.	Tanishima et al.	Ko et al.
Age (year)	33.8 (18-80)	≥ 18 (20-82)	36 (32-37-38)	43.2 (37-50)	Mean 33
No. and gender (M/F)	501 210/294	128/105	866 369/297	111 39/56/16%	2877 1947/930/4%
Ethnicity	American	Polish	Japanese	Chinese Indian 20%, Others 19%	Hong Kong Chinese
Baseline data	No	Yes	No	No	Yes
Prevalence of diabetes (%)	10.7	19	20.6	17	21
Results of tests					
HbA _{1c}					
Cut-off point (%)	≥ 5.1	≥ 6.6	≥ 5.5 > 6.0	≥ 6.9 > 7.4 > 7.6	≥ 6.9 > 7.4 > 7.6
Items			IGT DM	DM DCA 2000	DM DM
Se (%)	99	99	60.0 16.7	64.0 50.6 41.0	64.0 50.6 41.0
Sp (%)	99	99	87.0 92.9	91.0 98.2 100	91.0 98.2 100
Likelihood ratio					
PLR	379	379	1.33 2.35	7.11 26.11 --	7.11 26.11 --
NLR	0.26 0.66	M 0.31 F 0.60 M 2.12 F 4.86	0.73 0.90	0.40 0.50 0.59	0.40 0.50 0.59
FPG					
Cut-off point (mmol/l)	2.5-5 2.6-1	7.0 7.6	2.5-6 2.6-1	≥ 6.0 ≥ 6.7	≥ 6.0 ≥ 6.7
Items	DM DM	DM KGT	IGT	DM	
Se (%)	79.9 63.6	M 91 M 19	76.5 34.9	89.9 78.1	89.9 78.1
Sp (%)	79.9 93.9	M 30.0 M 19.3 F 21.6 F 9.3	87.9 86.9	65.9 87.9	65.9 87.9
Likelihood ratio					
PLR	3.98 10.4	1.30 3.73	1.23 2.65	2.64 6.45	2.64 6.45
NLR	0.25 0.59	0.31 2.12			
ROC curve available	No	Yes (for KGT)	Yes	Yes	Yes
Diagnose criteria	WHO 1999	WHO 1999	WHO 1999	WHO 24 OGTT and ADA (1997)	WHO 24 OGTT

HbA1c had higher sensitivity but lower specificity than FPG to diagnose diabetes at different cut-off points

Results by cut-off point

Cut-off point	HbA1c			FPG	
	≥ 5.9	≥ 6.1	≥ 6.2	≥ 6.1	≥ 5.6
SN (%)	76-95	78-81	43-81	48-64	80-88
SP (%)	67-86	79-84	88-99	94-98	79.2-85.8

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Conclusions

- HbA1c and FPG are both *equally effective* as screening tools in early detection of Type 2 diabetes, but neither of the tests is effective in detecting IGT
- OGTT is therefore still required to diagnose IGT.
- need for the standardization of HbA1c measurements worldwide to allow meaningful comparison of results across laboratories.

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Review: glycated haemoglobin A1c and fasting plasma glucose screening tests have similar sensitivities and specificities for early detection of type 2 diabetes

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Review: glycated haemoglobin A1c and fasting plasma glucose screening tests have similar sensitivities and specificities for early detection of type 2 diabetes

Operating characteristics of the HbA_{1c} and FPG tests for early detection of type 2 diabetes*

Diagnostic tests	Number of trials (n)	Cut-point	Sensitivity	Specificity	+LR	-LR
HbA _{1c}	1 (866)	≥5.9%	76%	86%	5.4	0.28
	1 (1111)		95%	67%	2.9	0.07
	1 (2877)	≥6.1%	78%	79%	3.7	0.29
	1 (1111)		81%	84%	5.1	0.23
	1 (505)	≥6.2%	43%	99%	107	0.38
	1 (1111)		81%	88%	6.8	0.22
FPG	1 (2877)	≥5.6 mmol/l	88%	79%	4.3	0.15
	1 (505)		80%	86%	5.6	0.24
	1 (1111)	≥6.1 mmol/l	48%	98%	24	0.53
	1 (10 447)		64%	94%	10	0.39

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Conclusions

- The HbA_{1c} and FPG screening tests have similar sensitivities and specificities for early detection of type 2 diabetes.
- The HbA_{1c} and FPG tests have lower sensitivities for detecting impaired glucose tolerance.

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Commentary

- Any single HbA_{1c} cut-point to rule in or rule out diabetes would lead to significant misdiagnosis. Hence, separate HbA_{1c} values may be needed:
 - one that clearly rules out diabetes mellitus and a higher HbA_{1c} value that clearly rules it in.
 - Patients with values between these thresholds would need to proceed to an OGTT.
 - At this time, clinicians should continue to use the current approach of screening high risk patients with an FPG test and recommending an OGTT if the value is >5.6 mmol/l.

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