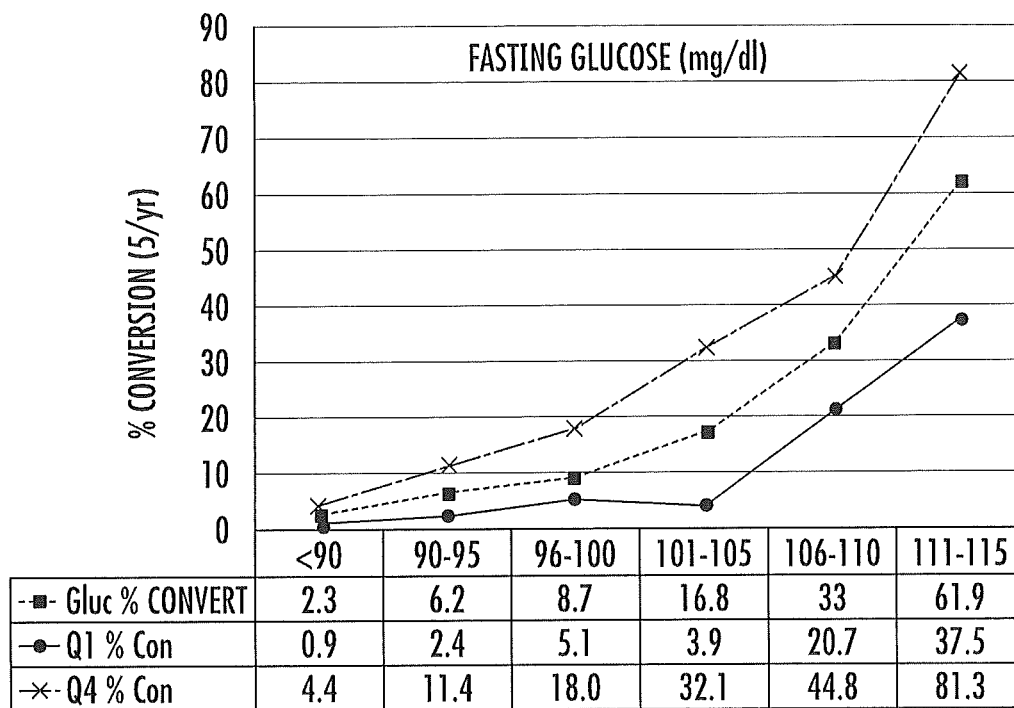
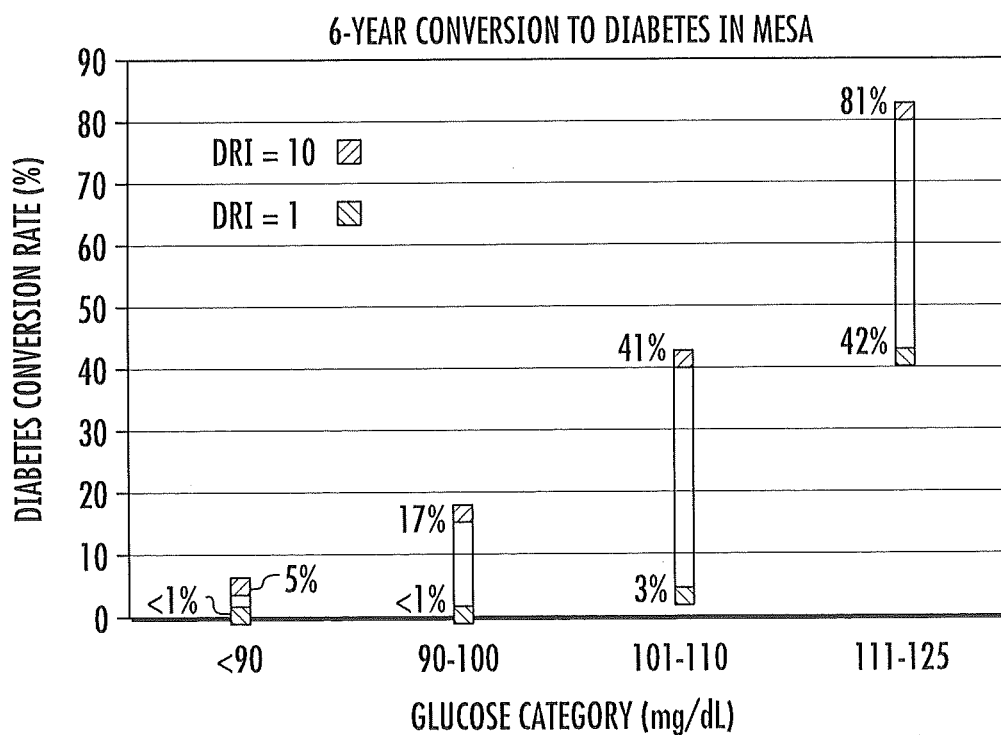


1/31

**FIG. 1A****FIG. 1B**

2/31

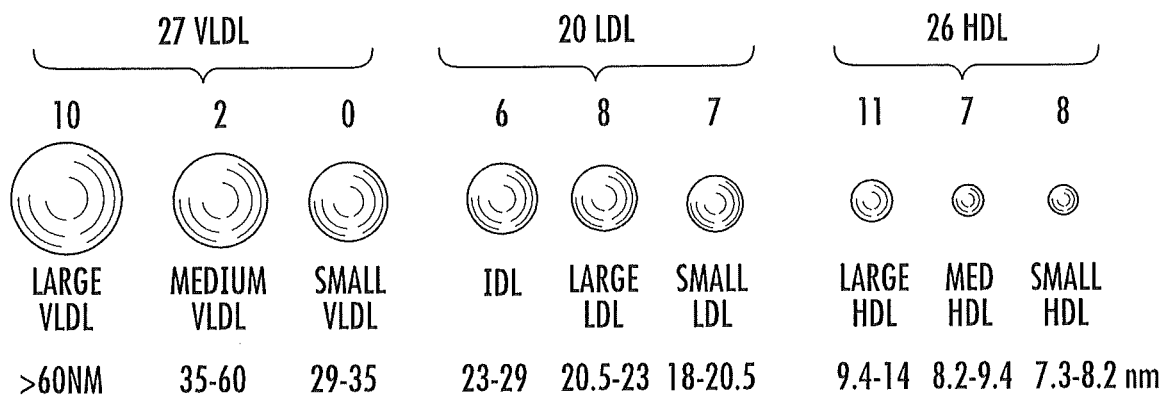


FIG. 2A

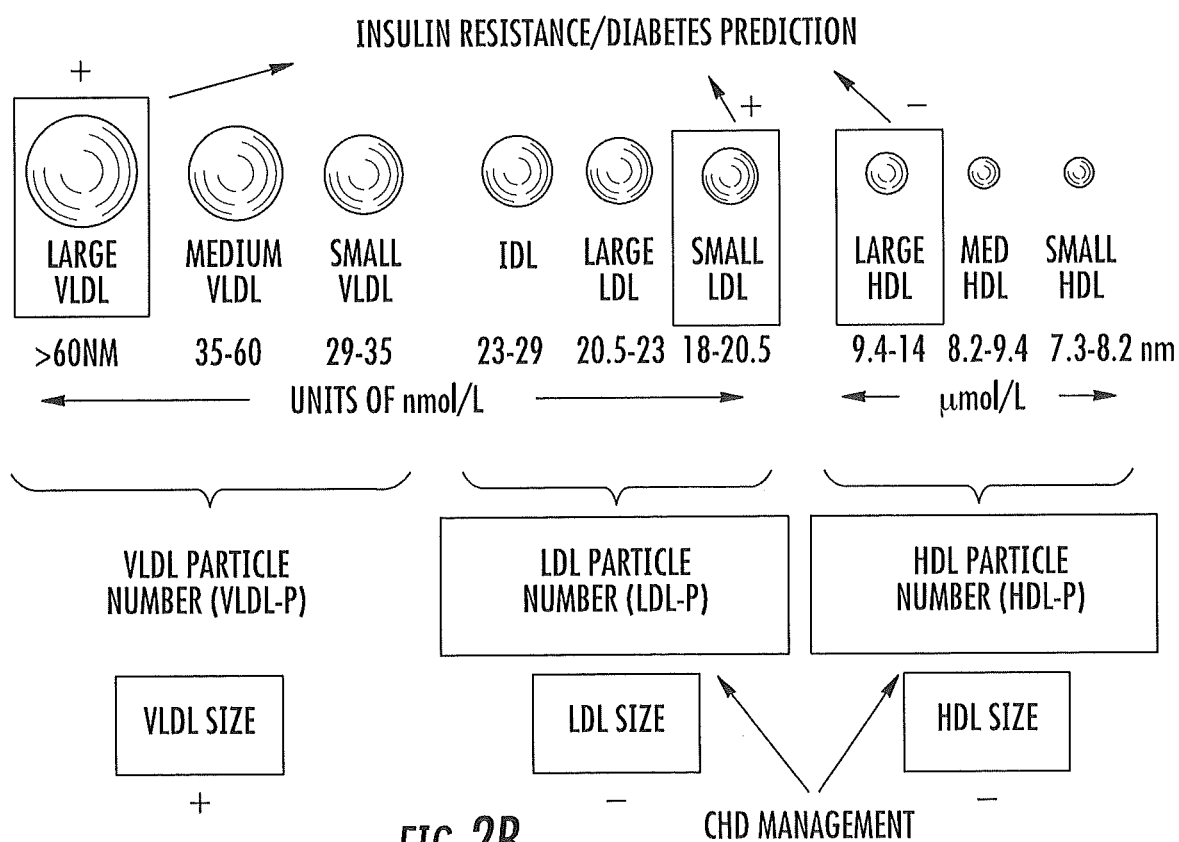


FIG. 2B

3/31

NMR HDL SUBPOPULATION GROUPINGS AND NOMENCLATURE FOR DIABETES RISK APPLICATIONS

HDL DECONVOLUTION MODEL COMPONENTS		HDL SUBPOPULATIONS			DM SUBCLASS GROUPINGS*	
COMPONENT NAME	ESTIMATED DIAMETER (nm)	COMPONENT NAME	SUBPOPULATION NAME	ESTIMATED DIAMETER (nm)	DESCRIPTIVE NAME	SUBCLASS NAMES
H1	7.4	H ₁₋₂	HP1	7.4-7.5	---	---
H2	7.5					
H3	7.6	H ₃₋₅	HP2	7.6-7.9	SMALL (7.6-8.2 nm)	H _S DM
H4	7.8					
H5	7.9					
H6	8.0	H ₆₋₈	HP3	8.0-8.2		
H7	8.1					
H8	8.2					
H9	8.3	H ₉₋₁₁	HP4	8.3-8.5	MEDIUM (8.3-10.2 nm)	H _M DM
H10	8.4					
H11	8.5					
H12	8.6	H ₁₂₋₁₄	HP5	8.6-9.3		
H13	9.0					
H14	9.2					
H15	9.4	H ₁₅₋₁₇	HP6	9.4-10.2		
H16	9.7					
H17	10.0					
H18	10.5	H ₁₈₋₂₀	HP7	10.3-10.9	LARGE (>10.2 nm) —	H _L DM
H19	10.6					
H20	10.8					
H21	11.0	H ₂₁₋₂₃	HP8	11.0-12.2		
H22	11.5					
H23	12.0					
H24	12.5	H ₂₄₋₂₆	HP9	12.3-13.5		
H25	13.0					
H26	13.5					

*SUBPOPULATION GROUPINGS AS GUIDED BY DIABETES RISK ASSOCIATIONS IN MESA.

FIG. 2C

4/31

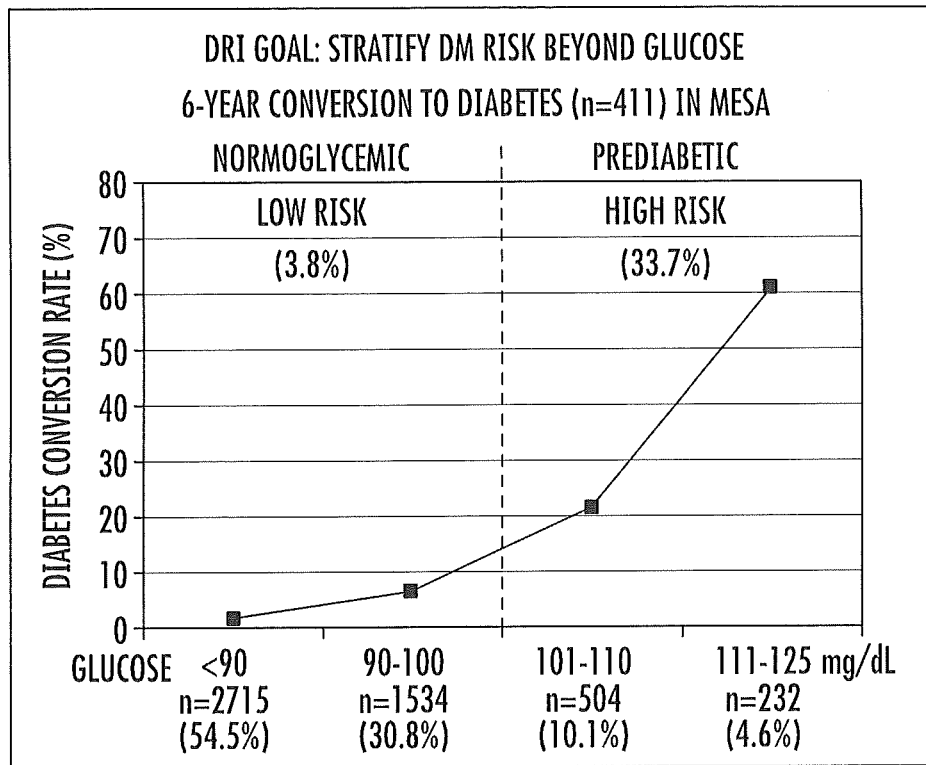


FIG. 3A

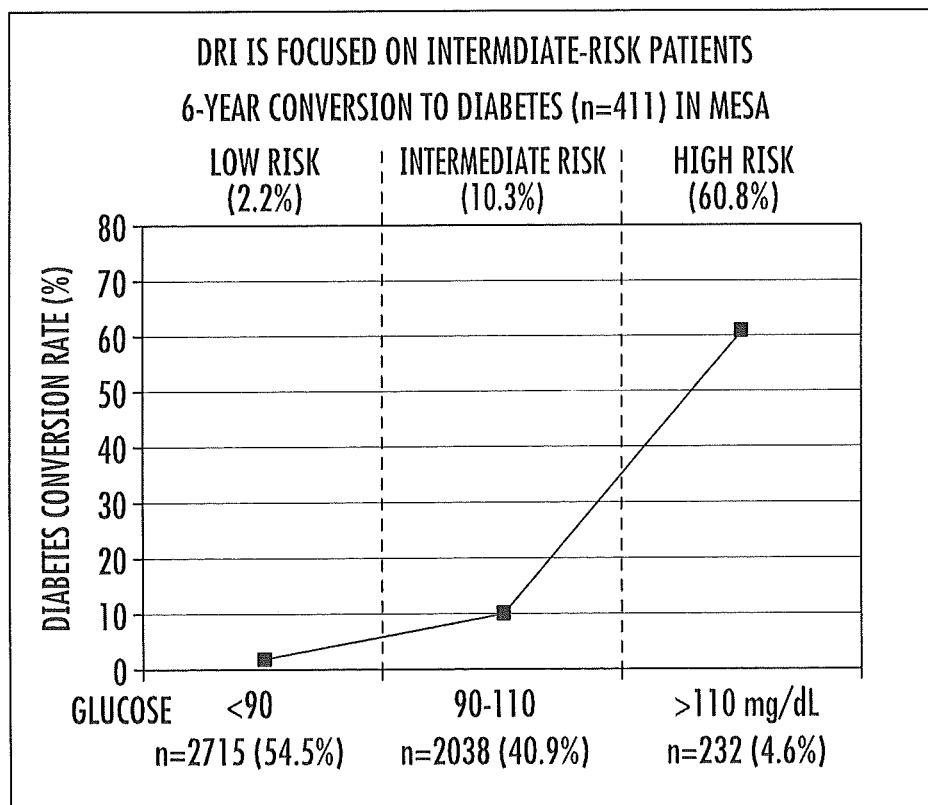


FIG. 3B

5/31

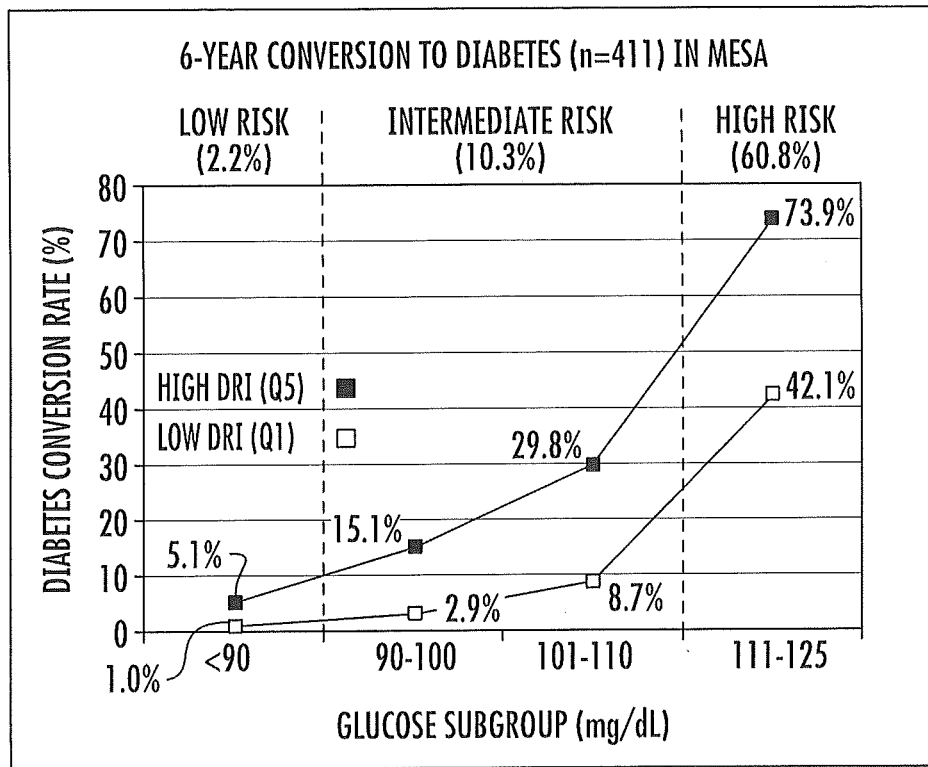


FIG. 4A

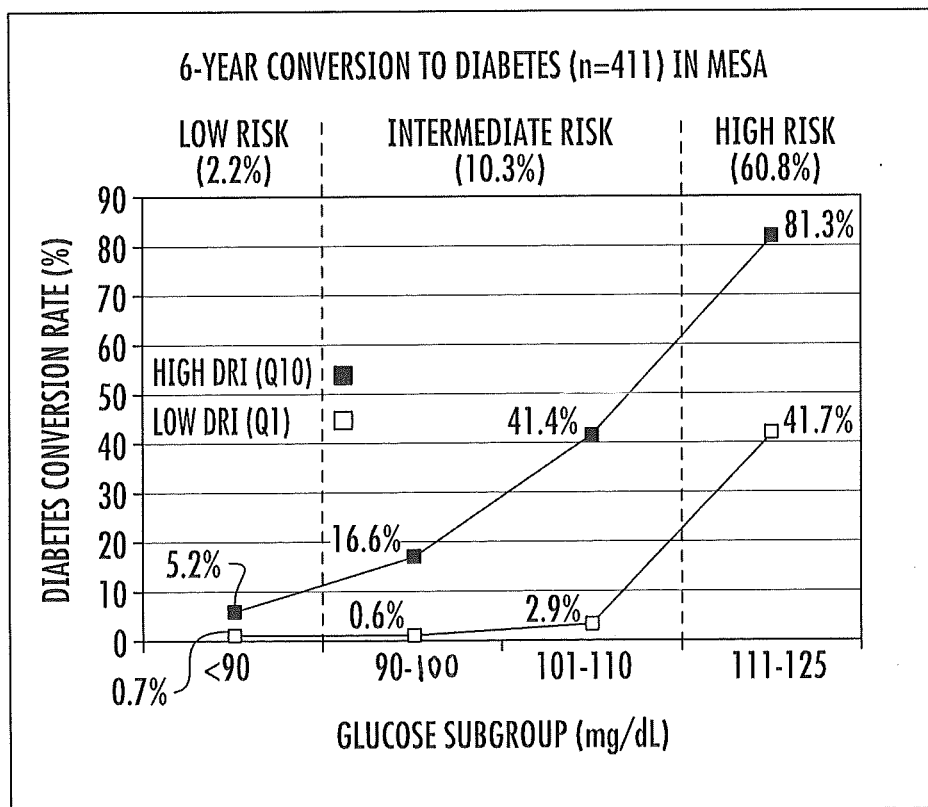


FIG. 4B

6/31

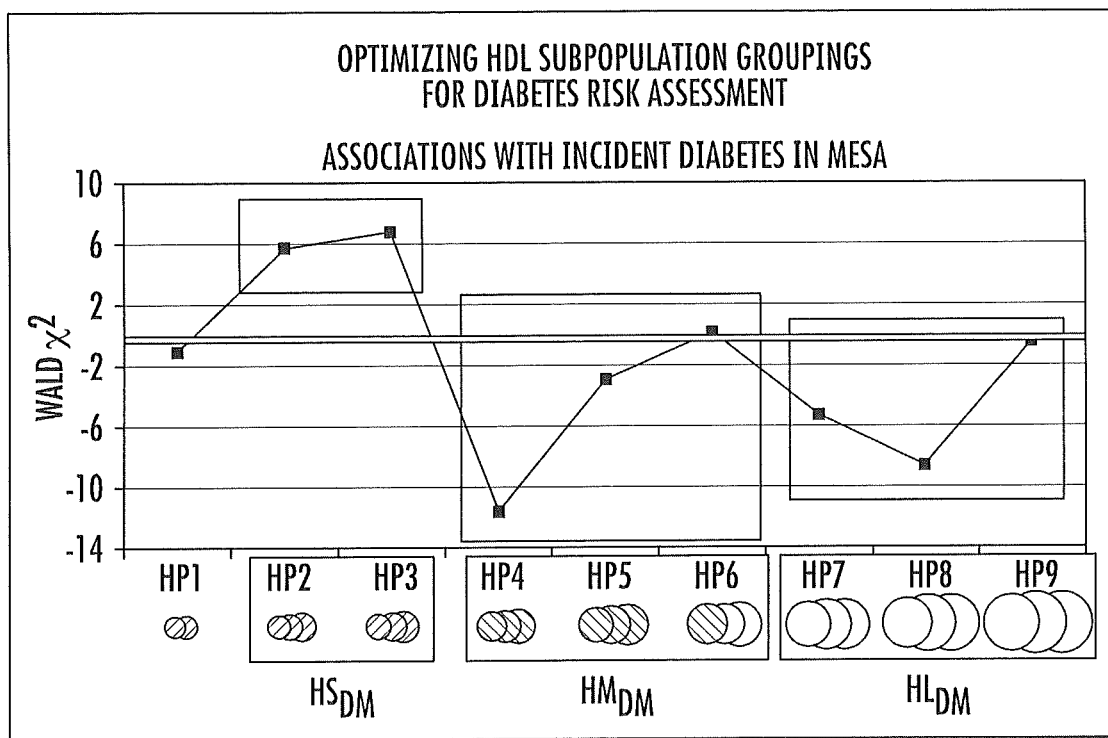


FIG. 5

**PROVISIONAL DRI PREDICTION MODEL
(SUBGROUP WITH GLUCOSE 90-110 mg/dL)**

	PROPOSED LINK TO PATHOPHYSIOLOGY	WALD χ^2	P
GLUCOSE		86.0	<0.0001
LP-IR	INSULIN RESISTANCE	18.0	<0.0001
HM x HZ	INSULIN SECRETION	16.5	<0.0001
GlycA	INFLAMMATION	6.1	0.01
GlycA x HM	INFLAMMATION	14.7	0.0001
VALINE	INSULIN RESISTANCE +/OR SECRETION (?)	2.9	0.09

FIG. 6

7/31

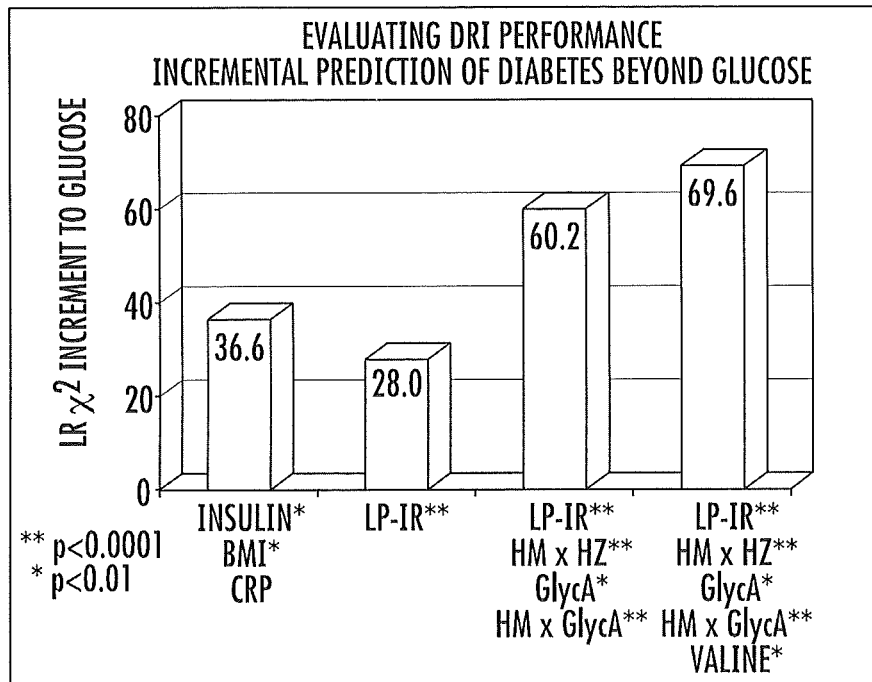


FIG. 7

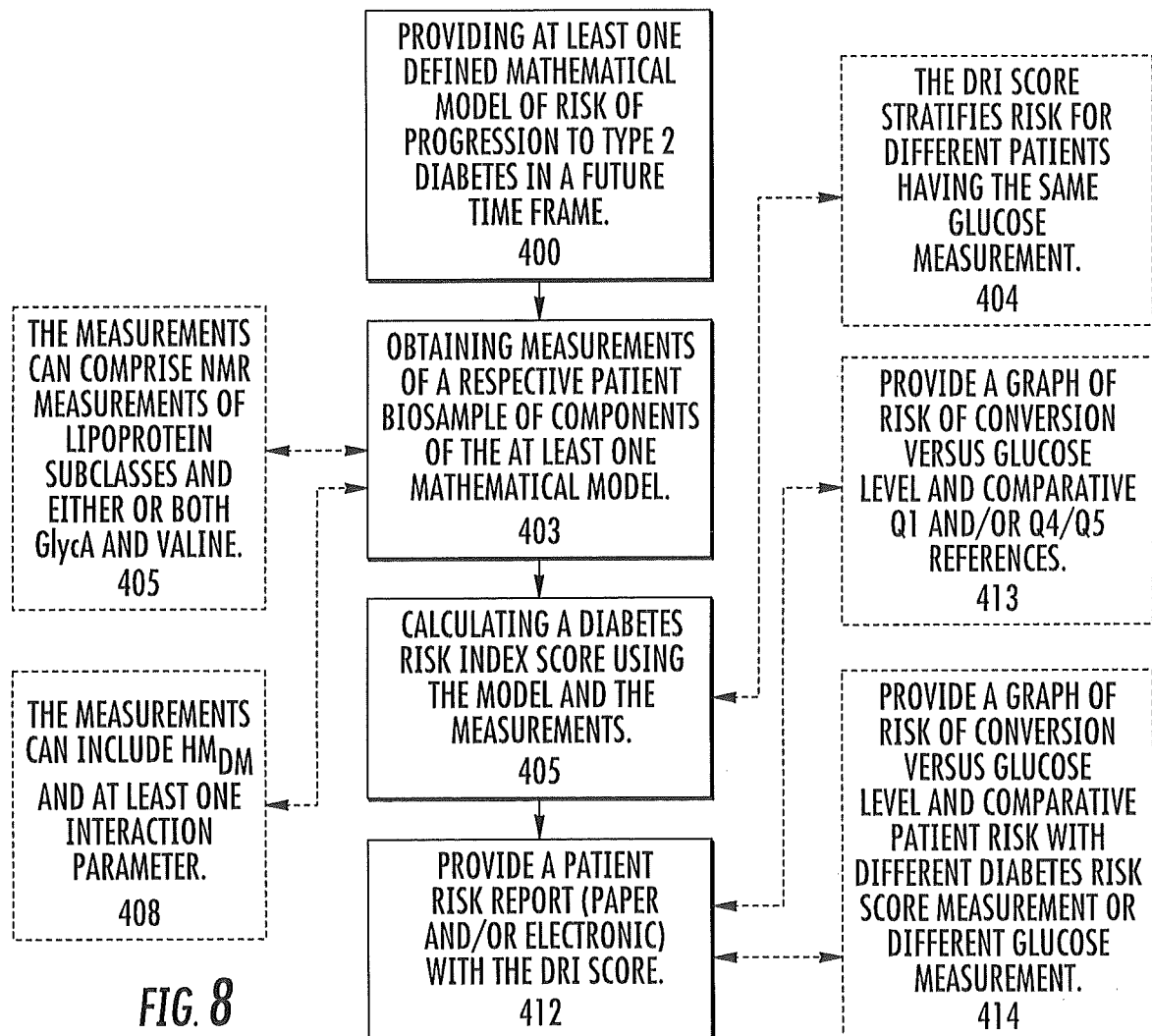
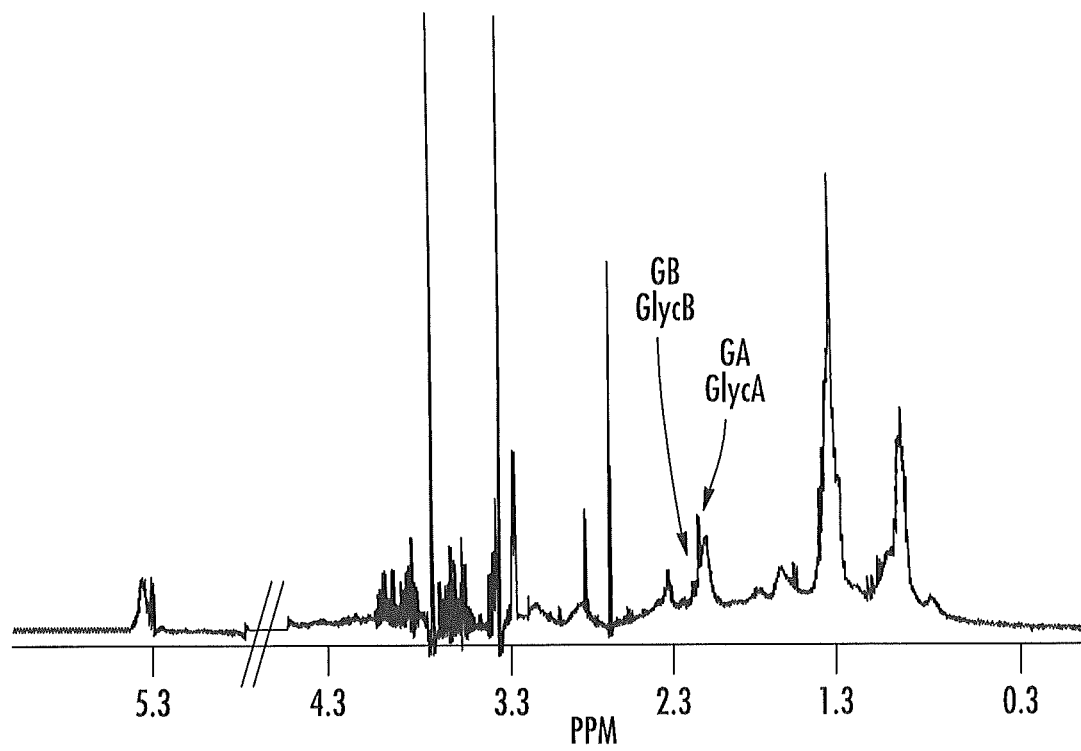
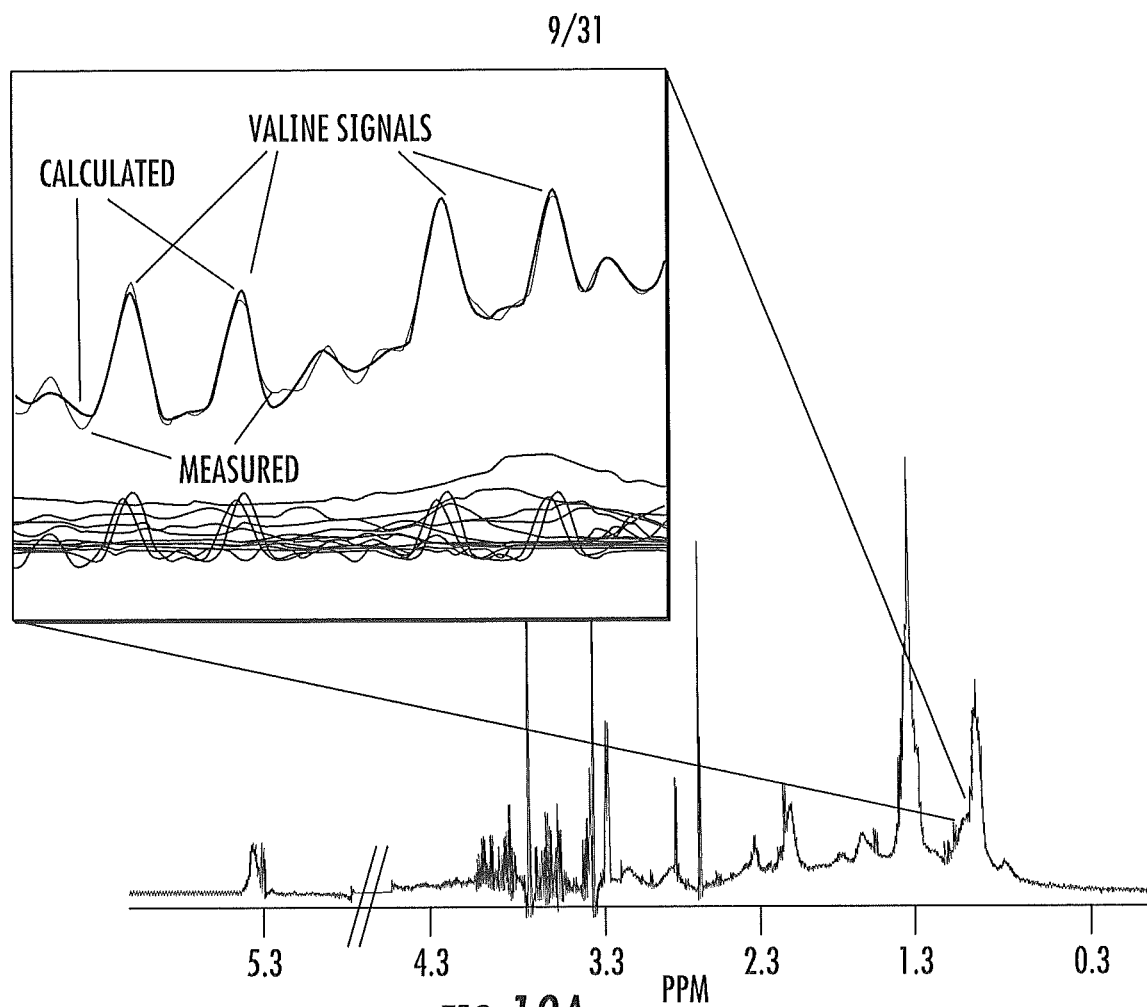
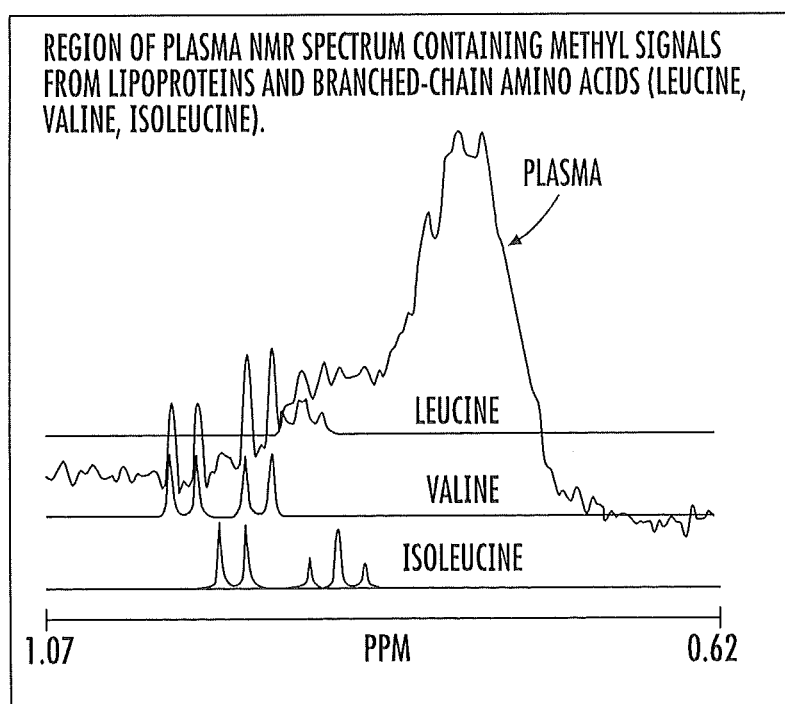


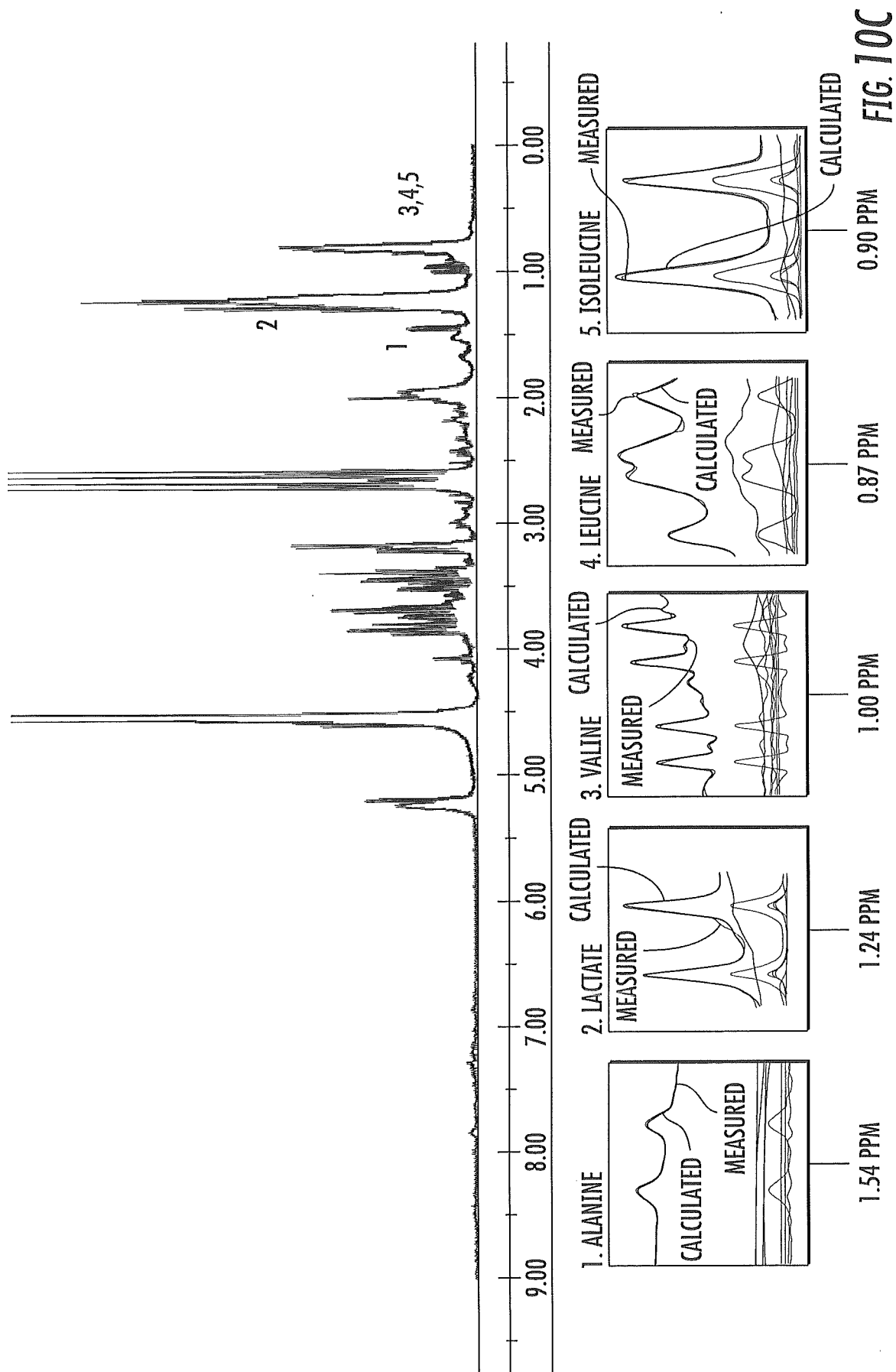
FIG. 8

8/31

**FIG. 9**

**FIG. 10A****FIG. 10B**

10/31



11/31

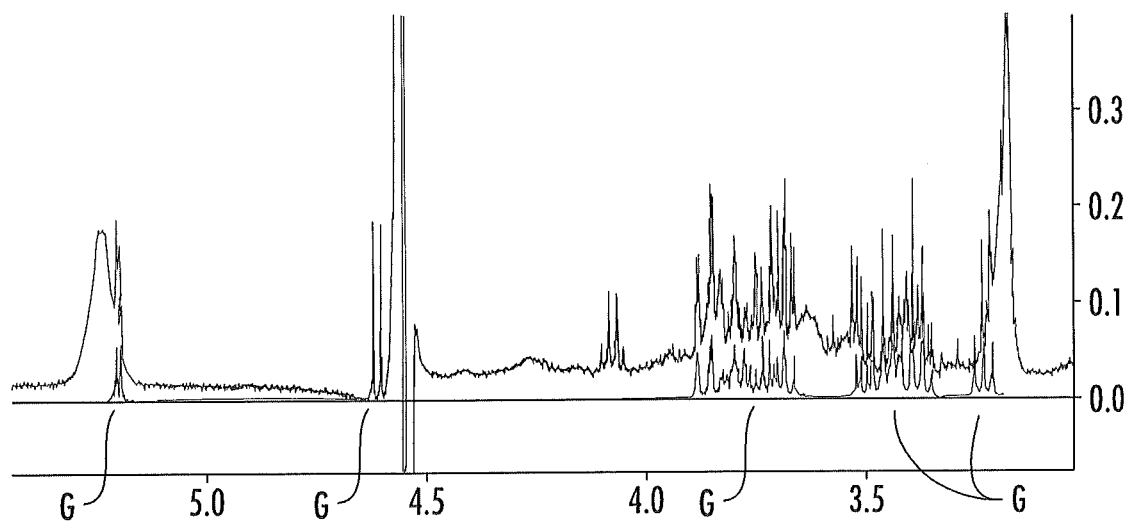


FIG. 11A

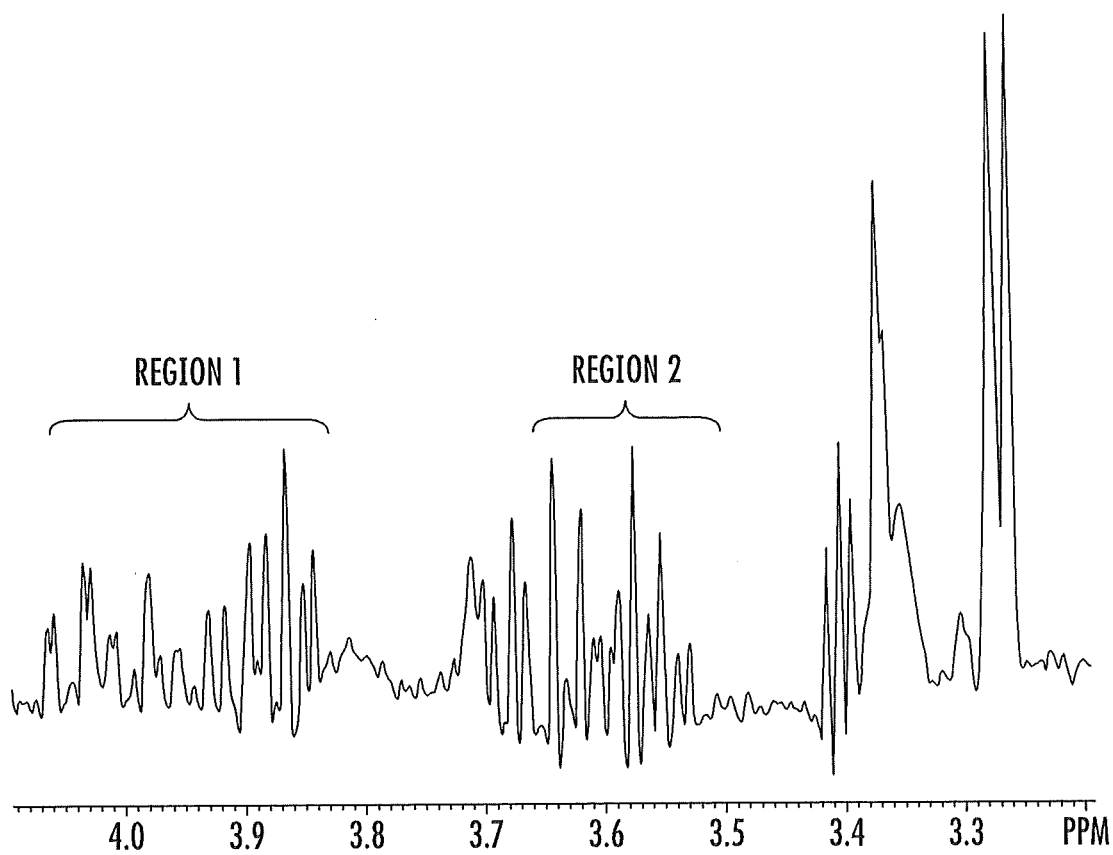
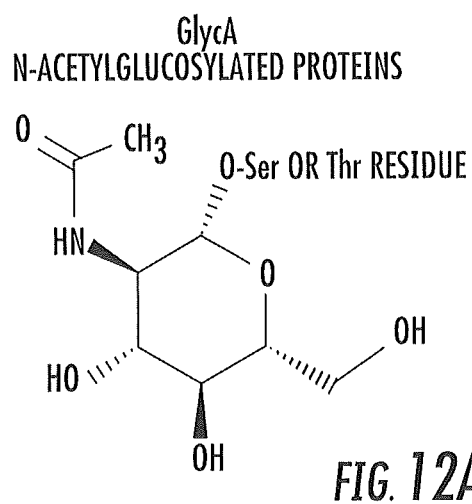


FIG. 11B

12/31



GlycA (FROM O- AND N-LINKED GLYCOPROTEINS)

β-D-N-ACETYLGLUCOSAMINE (GlcNAc)			GlcNAc
β-D-N-ACETYLGALACTOSAMINE (GalNAc)			GalNAc

FIG. 12B

13/31

GlycB
N-ACETYLNEURAMINIC ACID MODIFIED PROTEINS

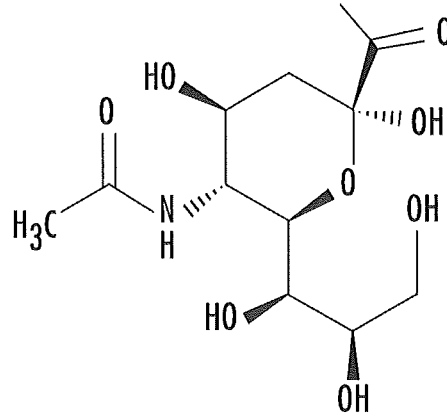


FIG. 13A

GlycB (FROM O- AND N-LINKED GLYCOPROTEINS)

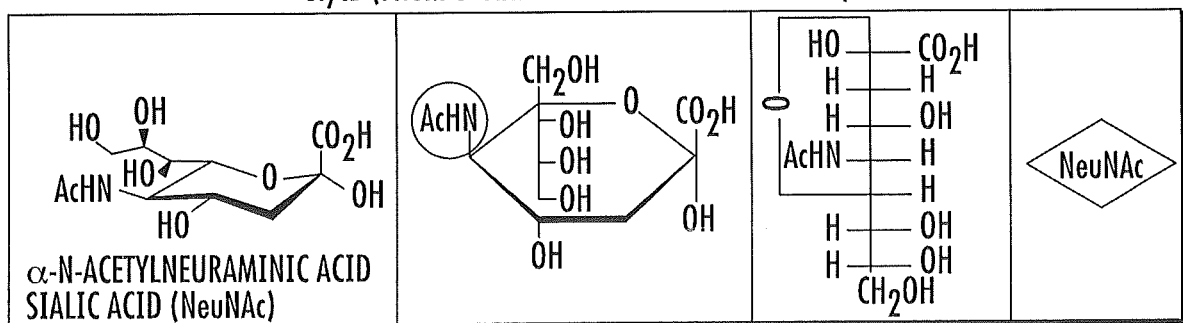
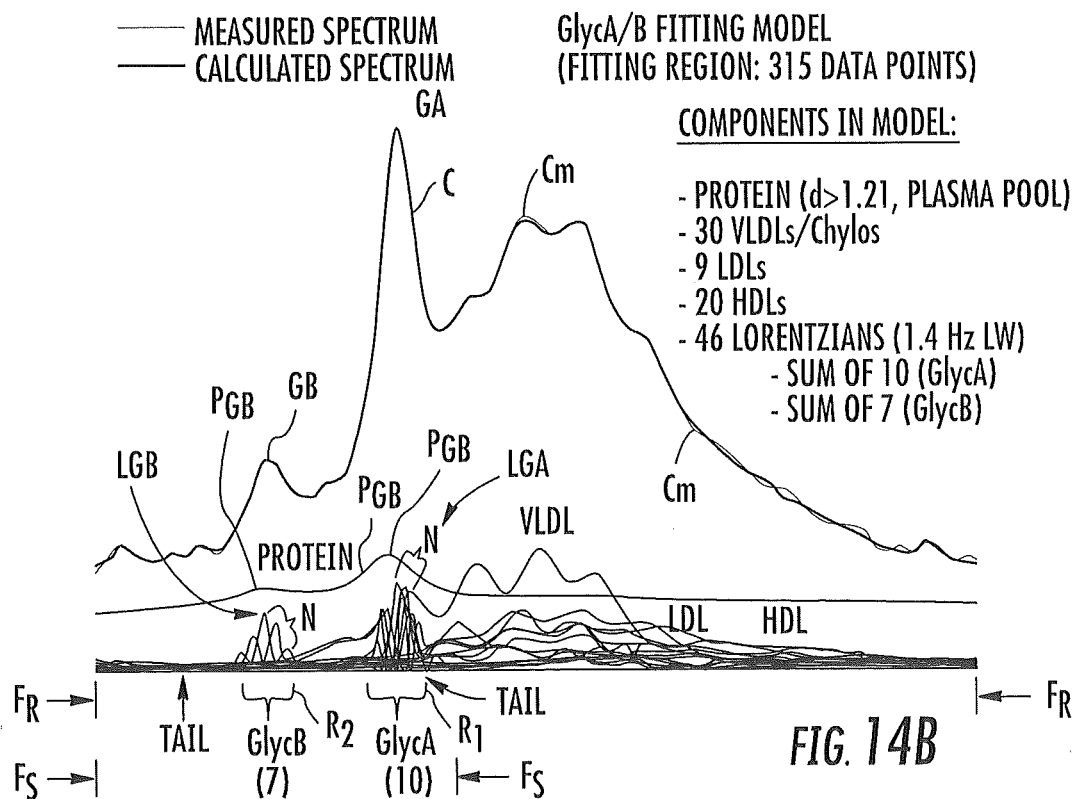
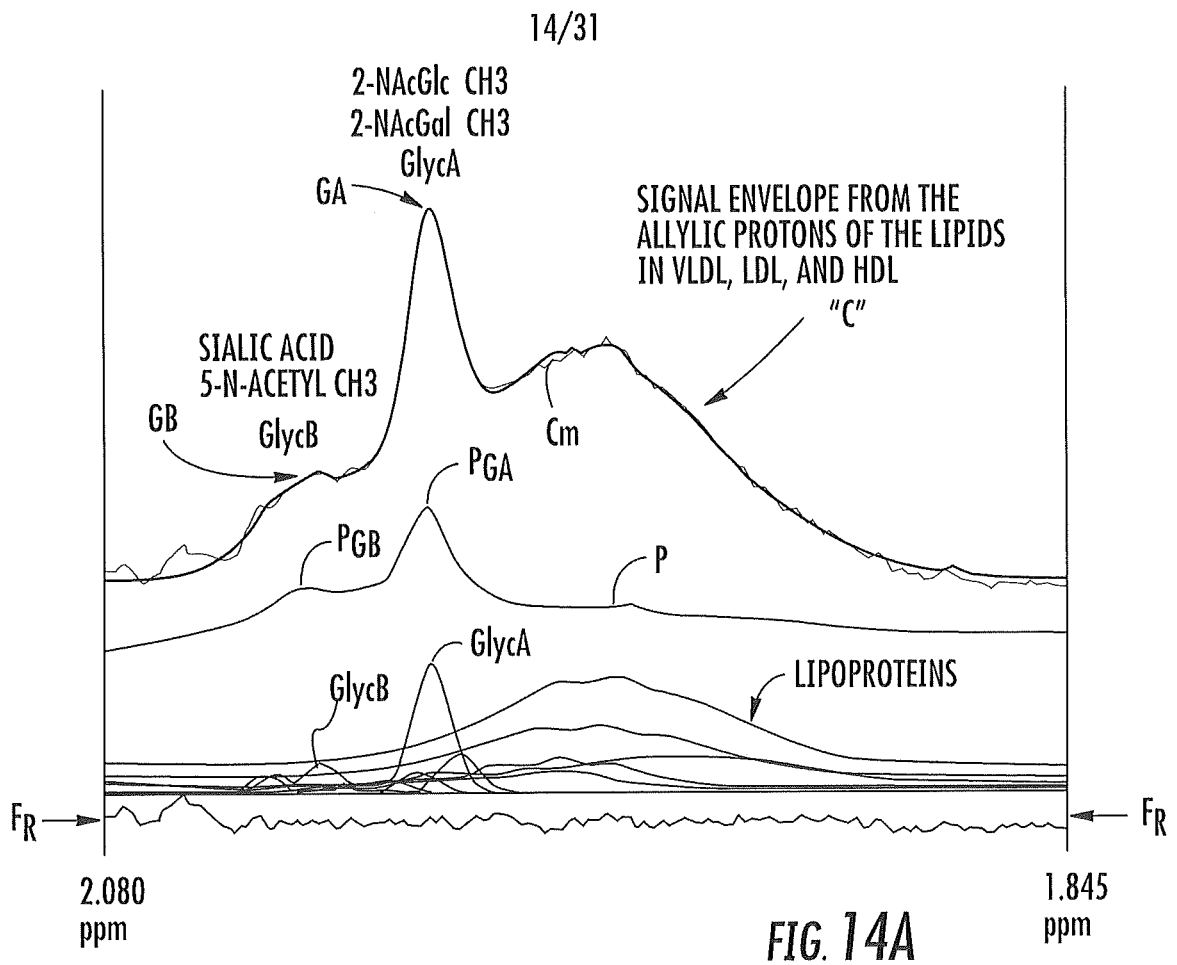
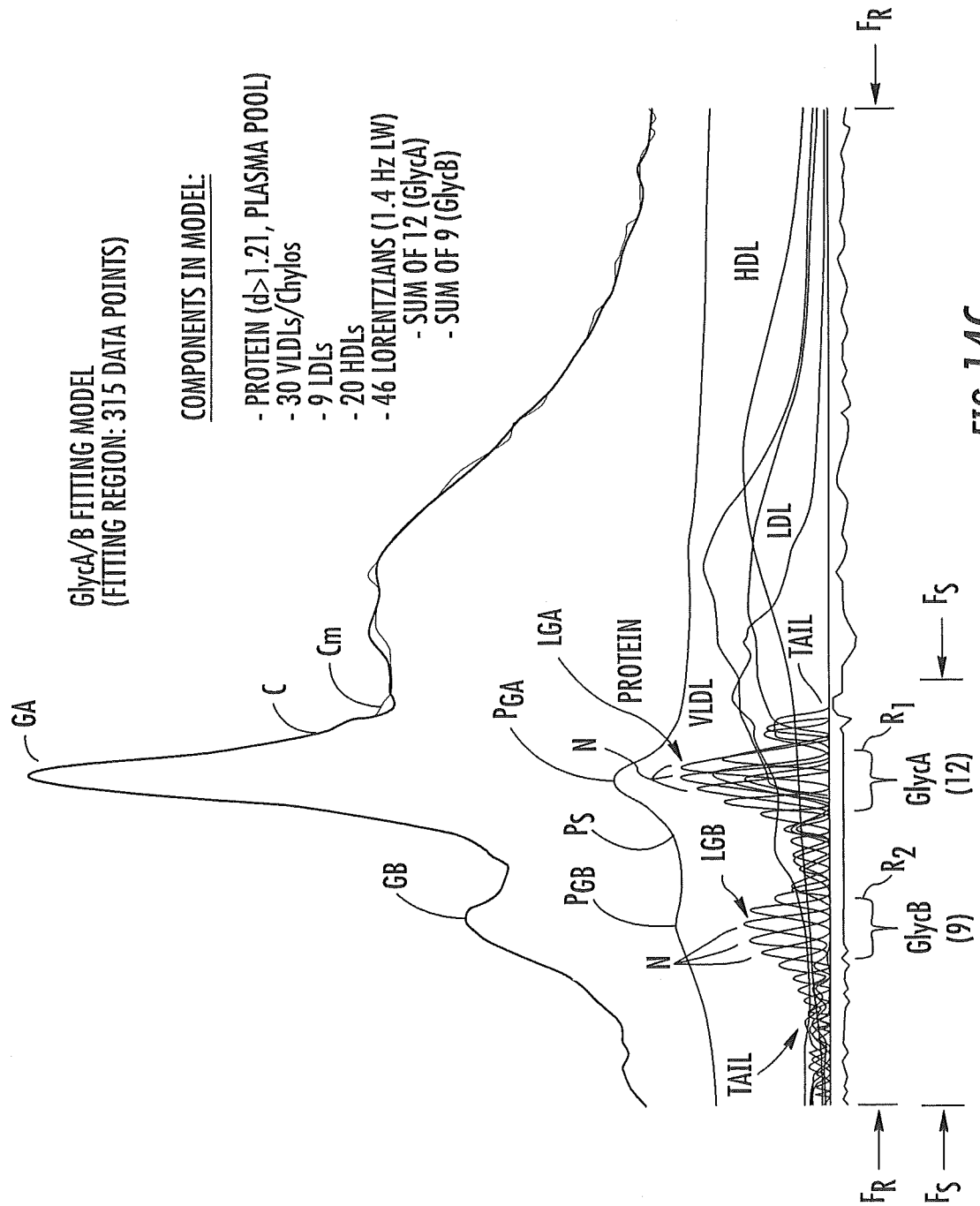


FIG. 13B



15/31



16/31

COMPONENT ID	COMPONENT CLASS	CHEMICAL SHIFT (PPM)	COMPONENT ID	COMPONENT CLASS	CHEMICAL SHIFT (PPM)	COMPONENT ID	COMPONENT CLASS	CHEMICAL SHIFT (PPM)
AA1	METABOLITE A	1.875040	VLDL7	VLDL	1.966840	GLYC21		2.019880
AA2	METABOLITE A	1.876400	VLDL8	VLDL	1.968200	GLYC22		2.021240
AA3	METABOLITE A	1.876400	VLDL9	VLDL	1.969560	GLYC23		2.022600
AA4	METABOLITE A	1.876400	VLDL10	VLDL	1.970920	GLYC24		2.023960
AA5	METABOLITE A	1.877760	VLDL11	VLDL	1.971600	GLYC25		2.025320
AA6	METABOLITE A	1.879120	VLDL12	VLDL	1.973640	GLYC26		2.026680
AA7	METABOLITE A	1.880480	VLDL13	VLDL	1.975000	GLYC27		2.028040
HDL1	HDL	1.915840	VLDL14	VLDL	1.976360	GLYC28		2.029400
HDL2	HDL	1.918560	VLDL15	VLDL	1.975680	GLYC29		2.030760
HDL3	HDL	1.919240	VLDL16	VLDL	1.977040	GLYC30		2.032120
HDL4	HDL	1.919920	CHY1	CHYLOS	1.978400	GLYC31		2.034840
HDL5	HDL	1.920600	CHY2	CHYLOS	1.979080	GLYC32		2.037560
HDL6	HDL	1.921280	CHY3	CHYLOS	1.979760	GLYC33		2.040280
HDL7	HDL	1.925360	CHY4	CHYLOS	1.980440	GLYC34		2.043000
HDL8	HDL	1.928760	CHY5	CHYLOS	1.981120	GLYC35		2.045720
HDL9	HDL	1.930800	CHY6	CHYLOS	1.981800	GLYC36		2.048440
HDL10	HDL	1.933520	CHY7	CHYLOS	1.982480	GLYC37		2.051160
HDL11	HDL	1.934880	CHY8	CHYLOS	1.983160	GLYC38		2.053880
HDL12	HDL	1.936240	CHY9	CHYLOS	1.983840	GLYC39		2.056600
HDL13	HDL	1.936920	CHY10	CHYLOS	1.984520	GLYC40		2.059320
HDL14	HDL	1.937600	CHY11	CHYLOS	1.985200	GLYC41		2.062040
HDL15	HDL	1.938280	CHY12	CHYLOS	1.985880	GLYC42		2.064760
HDL16	HDL	1.938960	GLYC1		1.992680	GLYC43		2.067480
HDL17	HDL	1.939640	GLYC2		1.994040	GLYC44		2.070200
HDL18	HDL	1.941000	GLYC3		1.995400	GLYC45		2.072920
HDL19	HDL	1.941680	GLYC4		1.996760	GLYC46		2.075640
HDL20	HDL	1.943040	GLYC5		1.998120	PROTEIN		
LDL1	LDL	1.947800	GLYC6		1.999480			
LDL2	LDL	1.948480	GLYC7		2.000840			
LDL3	LDL	1.949160	GLYC8		2.002200			
LDL4	LDL	1.949840	GLYC9		2.003560			
LDL5	LDL	1.950520	GLYC10		2.004920			
LDL6	LDL	1.951200	GLYC11		2.006280			
LDL7	LDL	1.952560	GLYC12		2.007640			
LDL8	LDL	1.953920	GLYC13		2.009000			
LDL9	LDL	1.955280	GLYC14		2.010360			
VLDL1	VLDL	1.960040	GLYC15		2.011720			
VLDL2	VLDL	1.961400	GLYC16		2.013080			
VLDL3	VLDL	1.962760	GLYC17		2.014440			
VLDL4	VLDL	1.964120	GLYC18		2.015800			
VLDL5	VLDL	1.965480	GLYC19		2.017160			
VLDL6	VLDL	1.966160	GLYC20		2.018520			

FIG. 14D

17/31

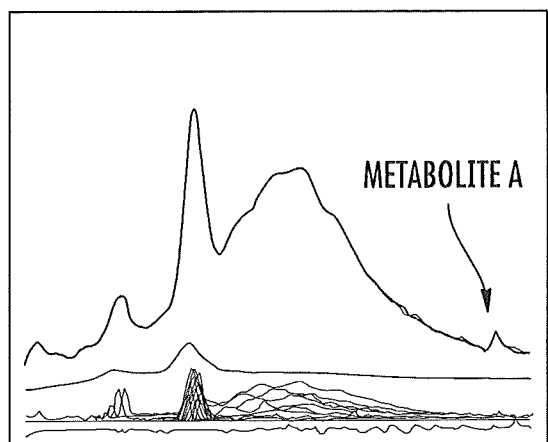


FIG. 14E

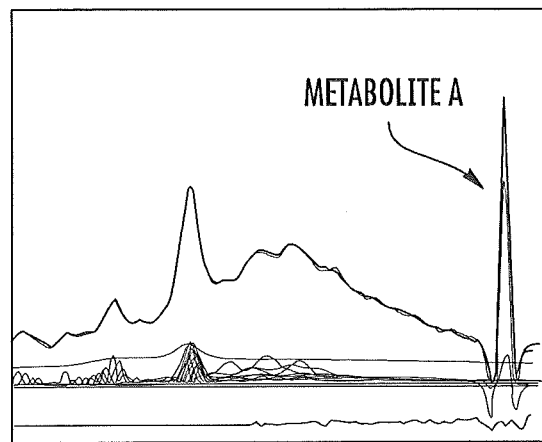


FIG. 14F

SPECTRAL OVERLAP FROM LIPOPROTEINS (ESPECIALLY VLDL/CHYLOS)
COMPLICATES ANALYSIS OF SAMPLES WITH HIGH TRIGLYCERIDES (TG)

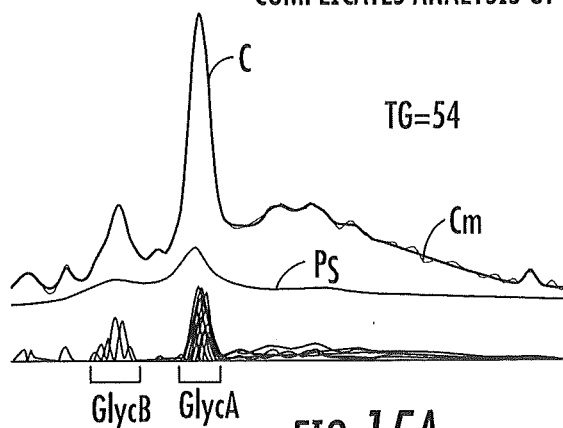


FIG. 15A

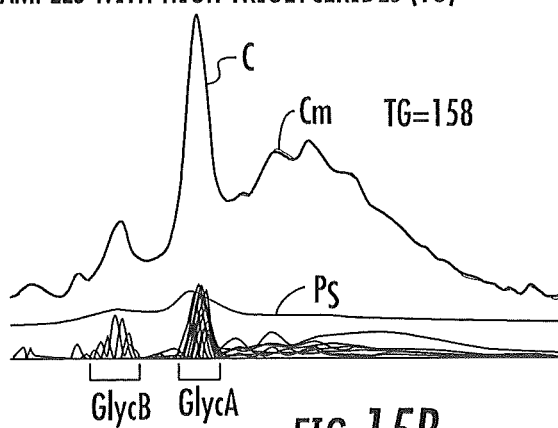


FIG. 15B

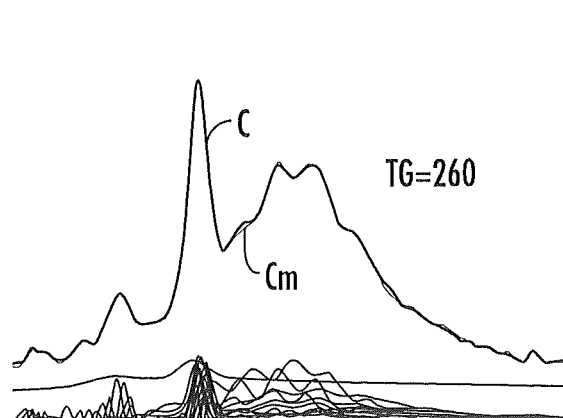


FIG. 15C

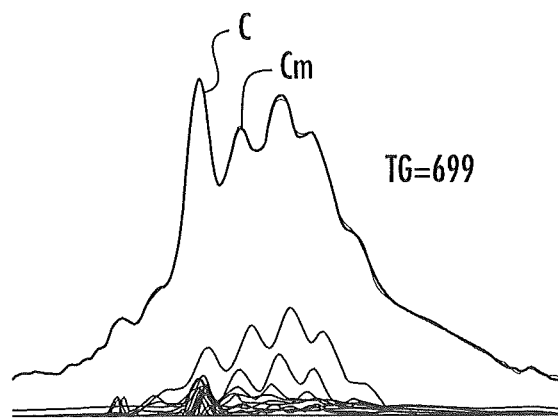


FIG. 15D

18/31

USE OF DIFFERENT PROTEIN COMPONENTS IN THE GlycA DECONVOLUTION MODEL GIVES DIFFERENT GlycA CONCENTRATIONS AND DIFFERENT GlycA ASSOCIATIONS WITH CHD EVENTS AND ALL-CAUSE DEATH IN MESA

PROTEIN COMPONENT USED IN FITTING MODEL	GlycA CONCENTRATION $\mu\text{mol/L}$	CHD EVENT PREDICTION		ALL-CAUSE DEATH PREDICTION	
		χ^2	p	χ^2	p
PROTEIN #1	342	13.1	0.0003	23.1	<0.0001
PROTEIN #2	186	12.7	0.0004	11.2	0.0008
PROTEIN #3	162	10.9	0.0003	7.4	0.007

FIG. 16A

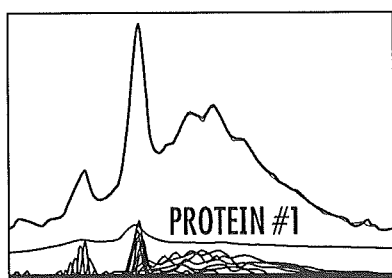


FIG. 16B

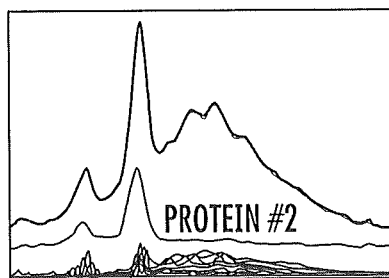


FIG. 16C

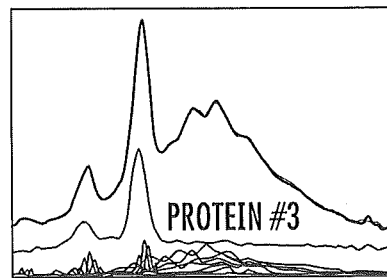


FIG. 16D

GlycA CONVERSION FACTOR GIVES
CONCENTRATION OF GLYCOPROTEIN N-ACETYL METHYL GROUPS

1 GlycA/B UNIT = 17.8 $\mu\text{mol/L}$

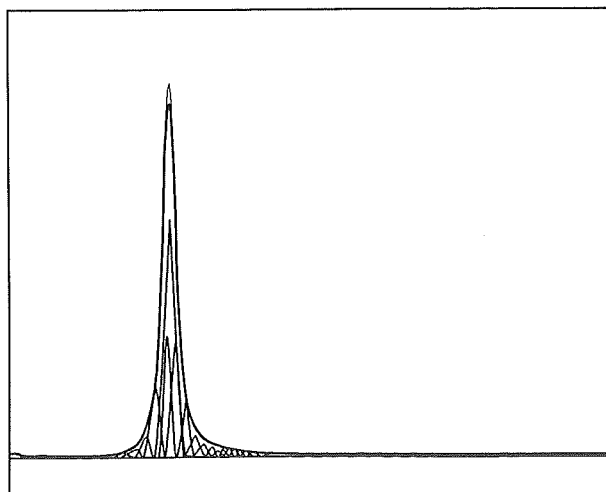
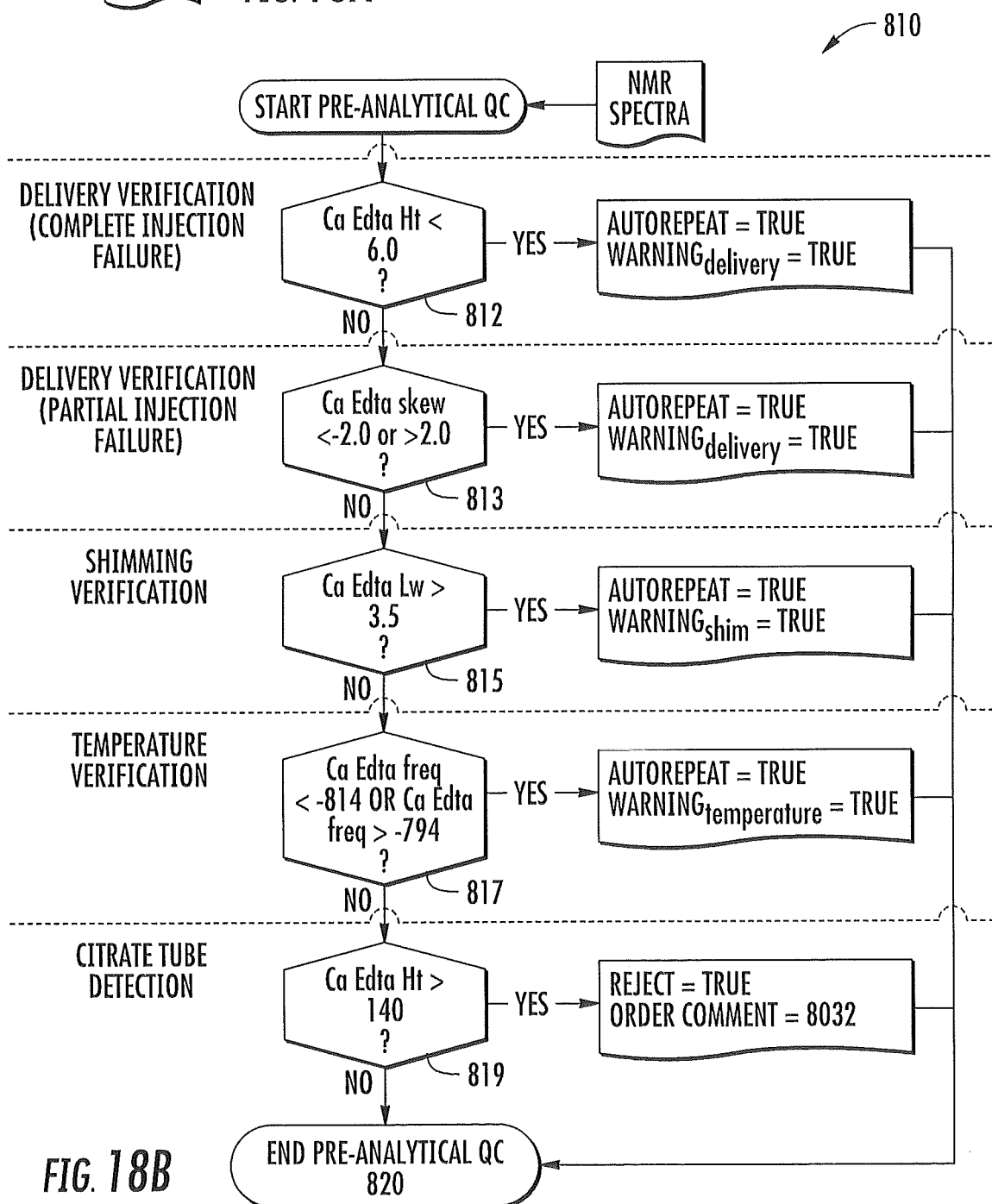
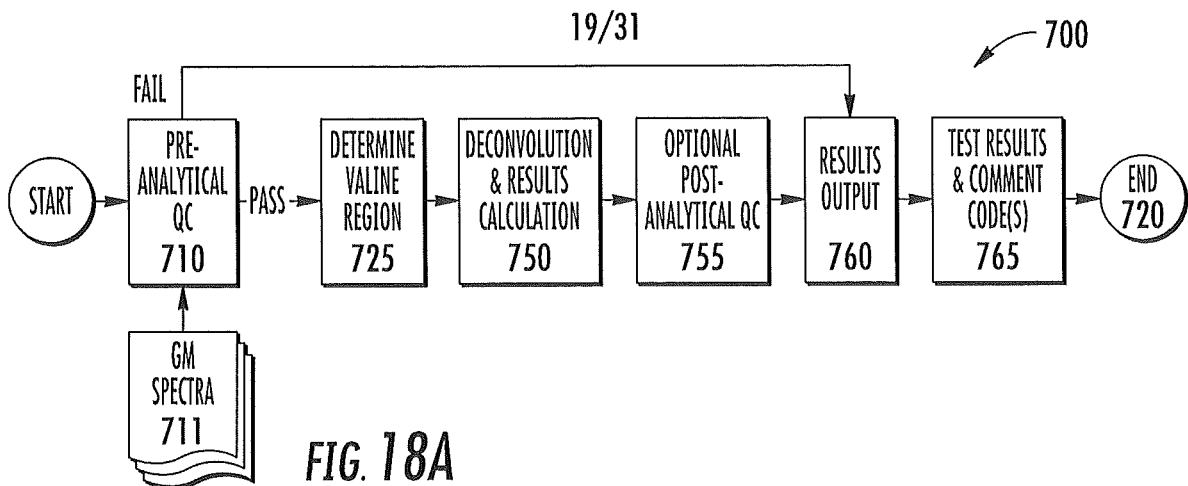


FIG. 17



20/31

900

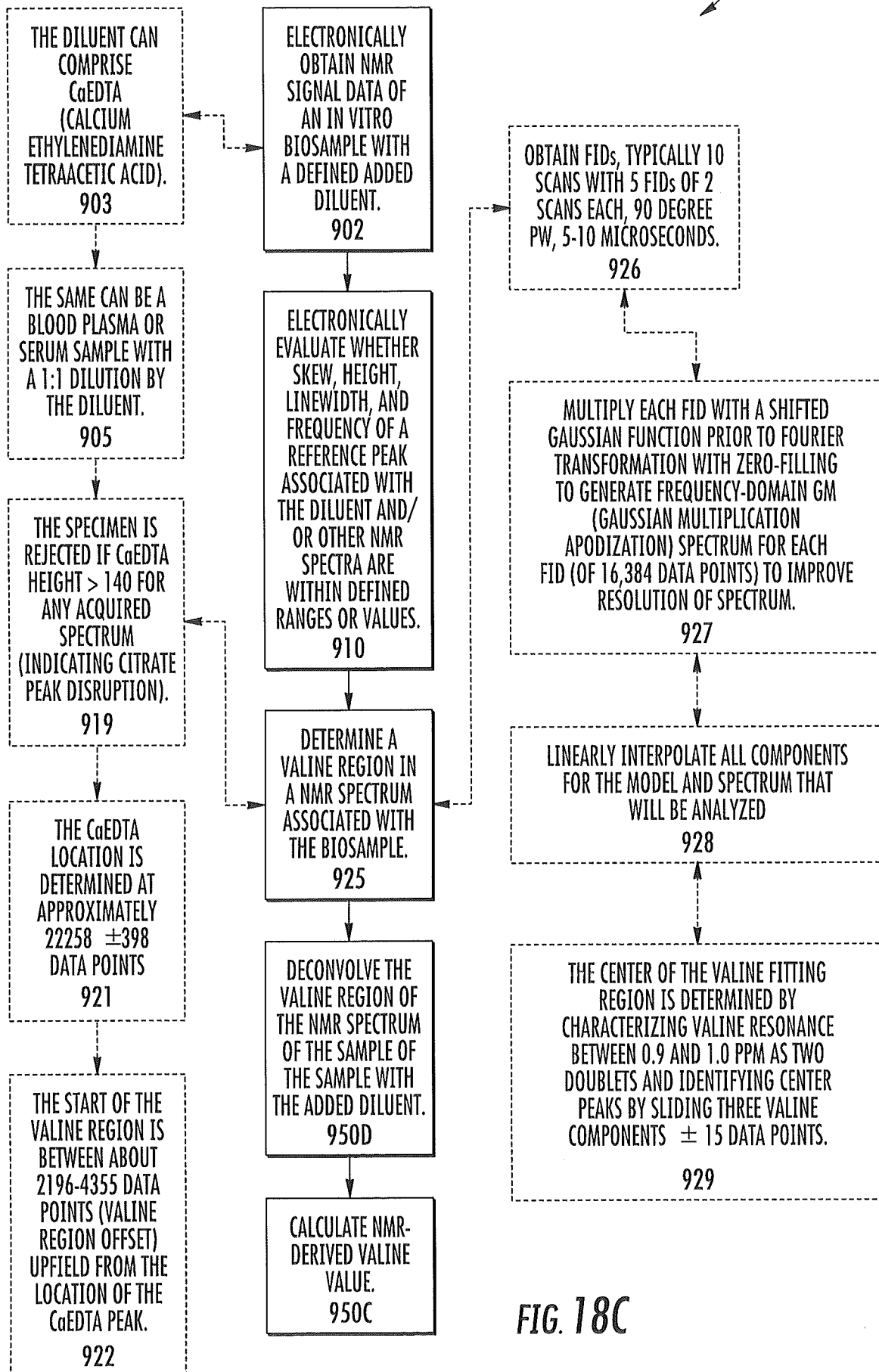


FIG. 18C

21/31

PROSPECTIVE ASSOCIATIONS OF NMR-MEASURED GlycA AND VALINE LEVELS AND HS-CRP WITH
SELECTED DISEASE OUTCOMES IN MESA (n~5680)

	GlycA		hs-CRP		VALINE		GlycA+VALINE
	χ^2	p	χ^2	p	χ^2	p	χ^2
CHD EVENTS (N=289)	7.0	0.007	3.1	ns	0.3	ns	7.8
ALL-CAUSE DEATH (N=346)	24.8	<0.0001	13.9	0.0003	14.4	0.0002	36.7
CONGESTIVE HEART FAILURE (N=149)	2.5	ns	2.9	ns	12.3	0.0006	14.1
STROKE (N=117)	1.3	ns	0	ns	0	ns	1.4
CHRONIC KIDNEY DISEASE (N=181)	29.3	<0.0001	3.4	0.05	2.9	ns	31.0
COPD (N=120)	20.5	<0.0001	3.6	0.03	6.7	0.01	26.3
CANCER (N=440)	8.0	0.004	3.0	ns	3.8	0.05	11.3
ASTHMA (N=154)	3.5	0.06	1.6	ns	2.0	ns	6.2
DEMENTIA (N=71)	5.8	0.01	0	ns	3.9	0.05	10.0
DIABETES (N=493)	10.3	0.001	4.7	0.04	29.0	<0.0001	40.3

FIG. 19

CHARACTERISTICS OF MESA SUBJECTS BY GlycA QUARTILE

	GlycA QUARTILE			
	1	2	3	4
GlycA	21.6	25.8	29.3	35.3
hsCRP (mg/L)	1.3	2.2	3.8	7.6
SMOKING (%)	9	11	13	17
HYPERTENSION (%)	34	41	47	55
DIABETES (%)	8.1	10.8	12.8	18.8
MetSyn (%)	20	31	39	55
LP-IR SCORE	35	44	46	52

FIG. 20

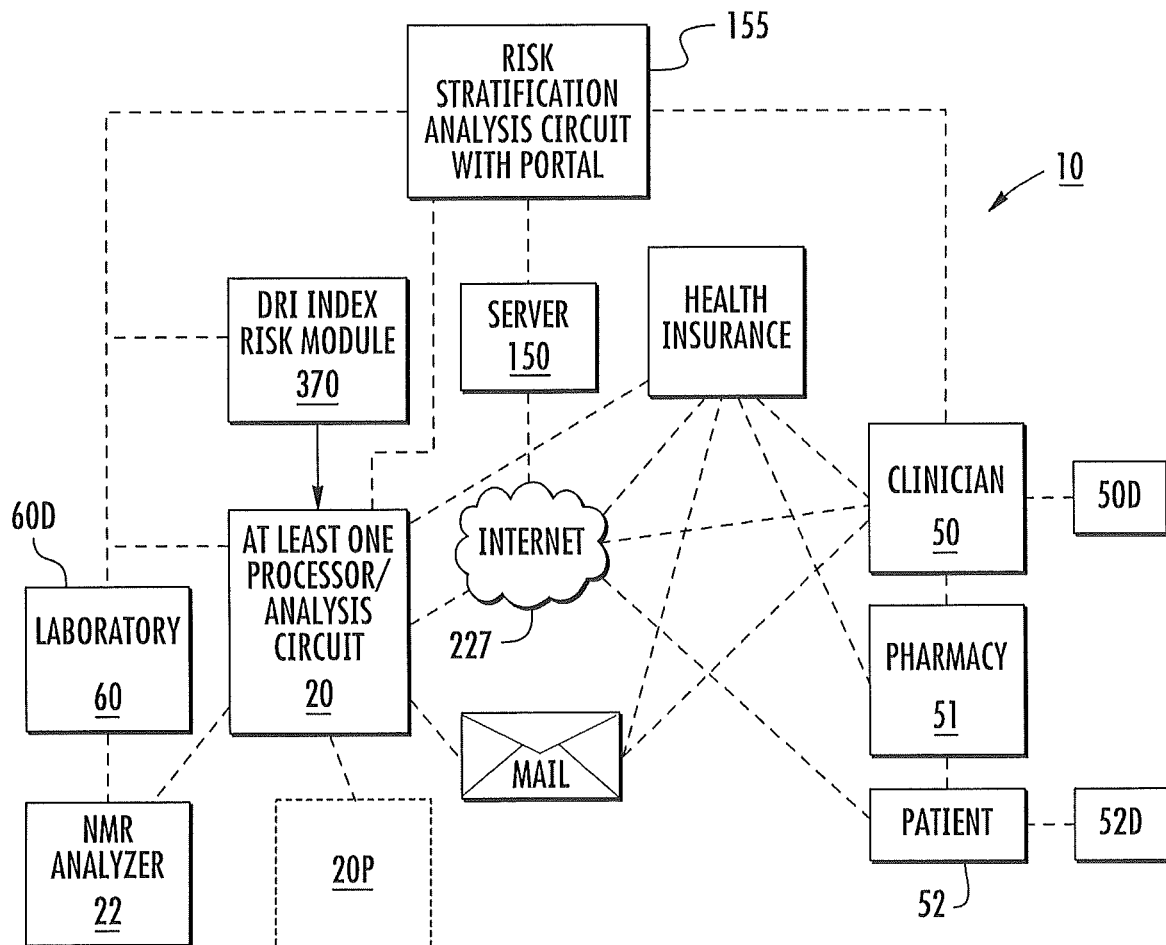
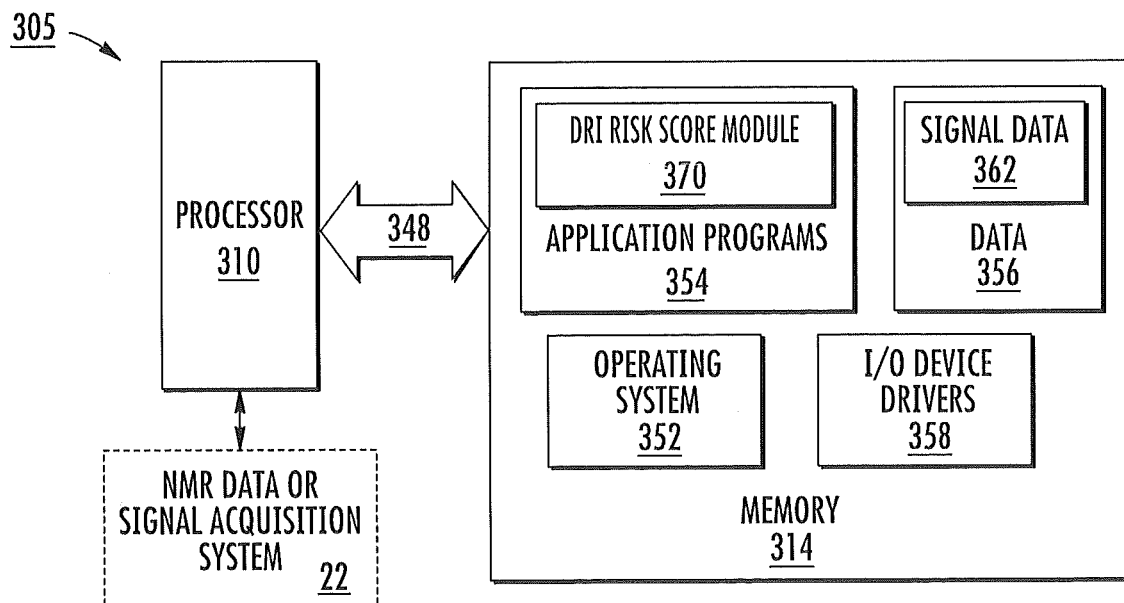
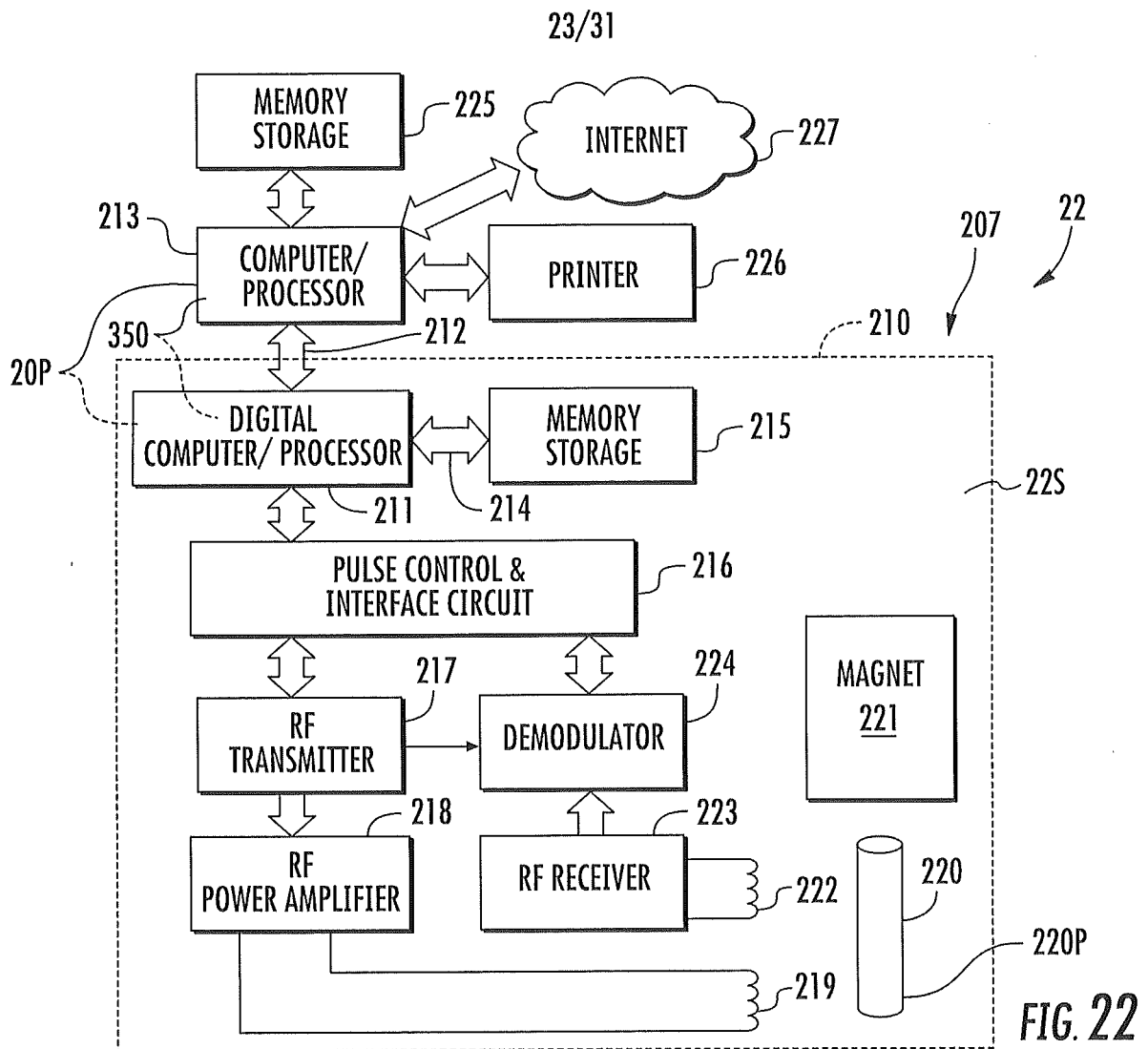


FIG. 21



24/31

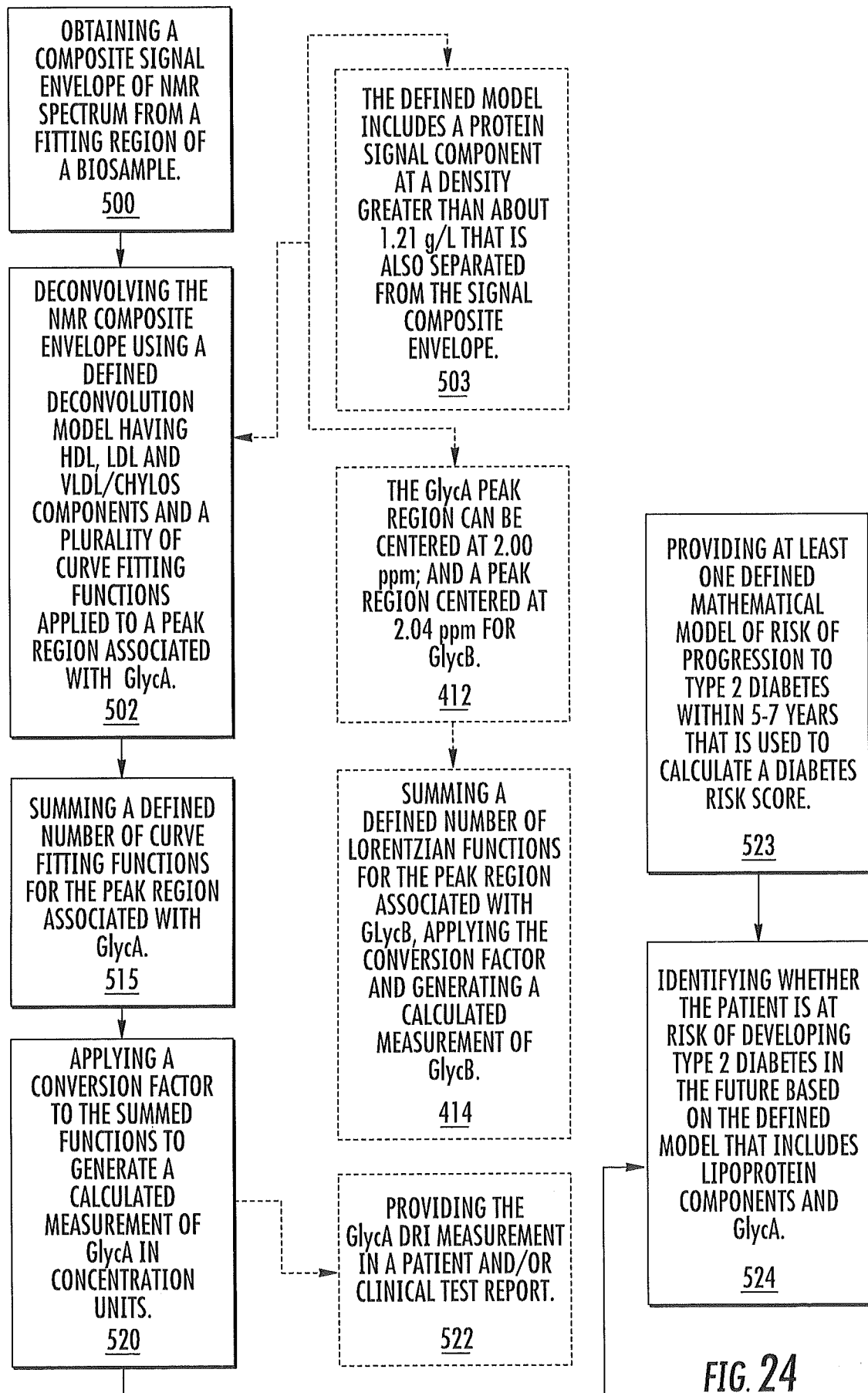


FIG. 24

25/31

100

PATIENT _____

HDL-P _____

LDL-P _____

GlycA _____

LOW HIGH

N₁ N₂

DRI

N#

101

101S

101

FIG. 25A

OPTION #1

FPG: 108 mg/dL

DRI SCORE: 32% RISK OF DEVELOPING T2D OVER NEXT 5 YEARS

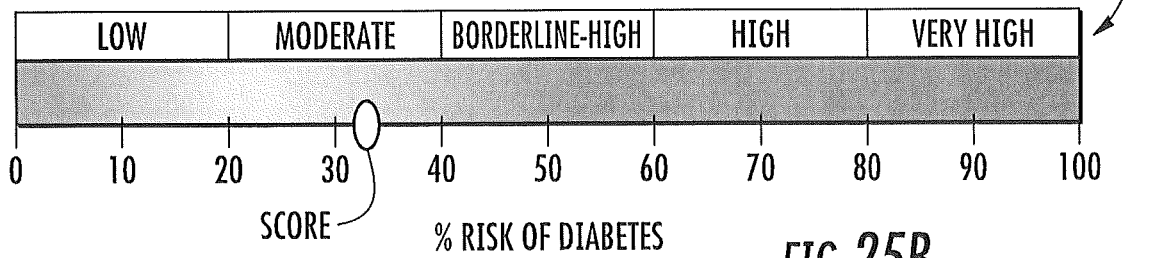
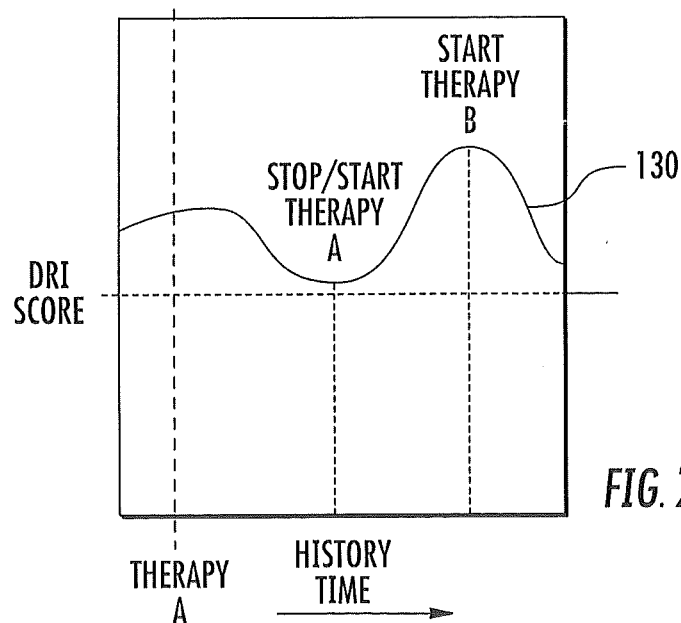
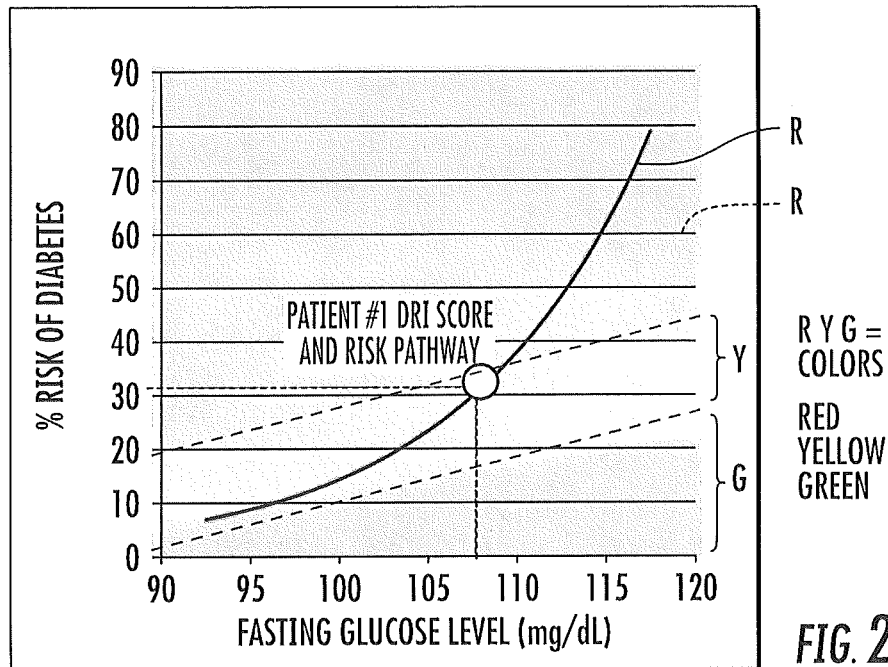


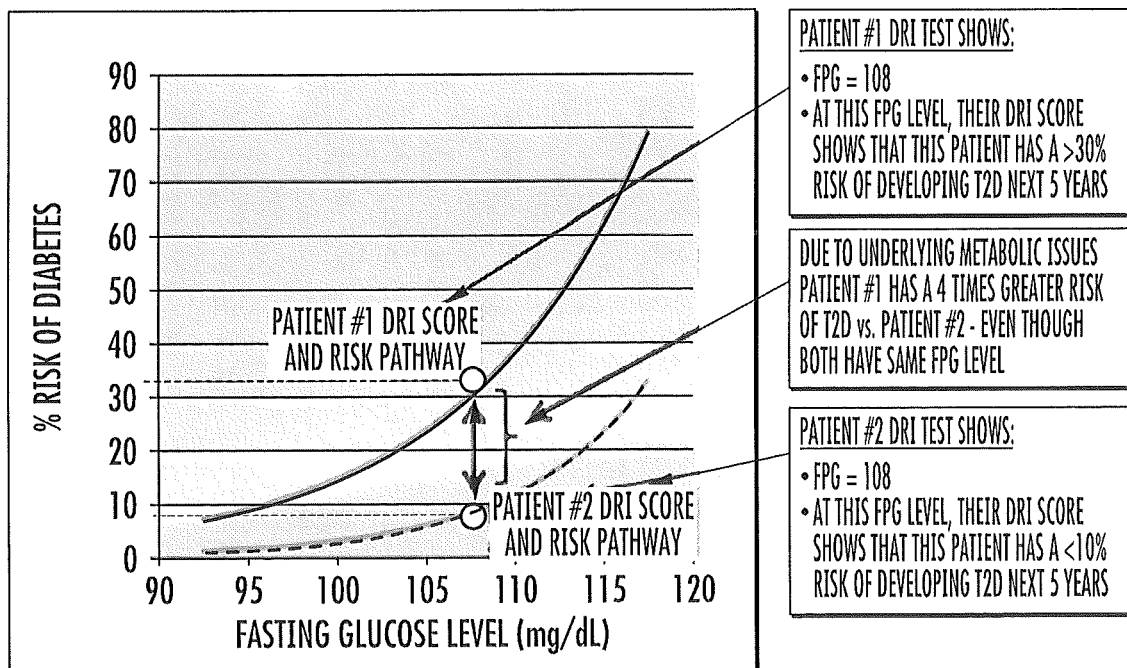
FIG. 25B



26/31

OPTION #2FPG: 108 mg/dLDRI SCORE: 32% RISK OF DEVELOPING T2D OVER NEXT 5 YEARSOPTION #2

FPG: 108 mg/dL

DRI SCORE: 32% RISK OF DEVELOPING T2D OVER NEXT 5 YEARS

27/31

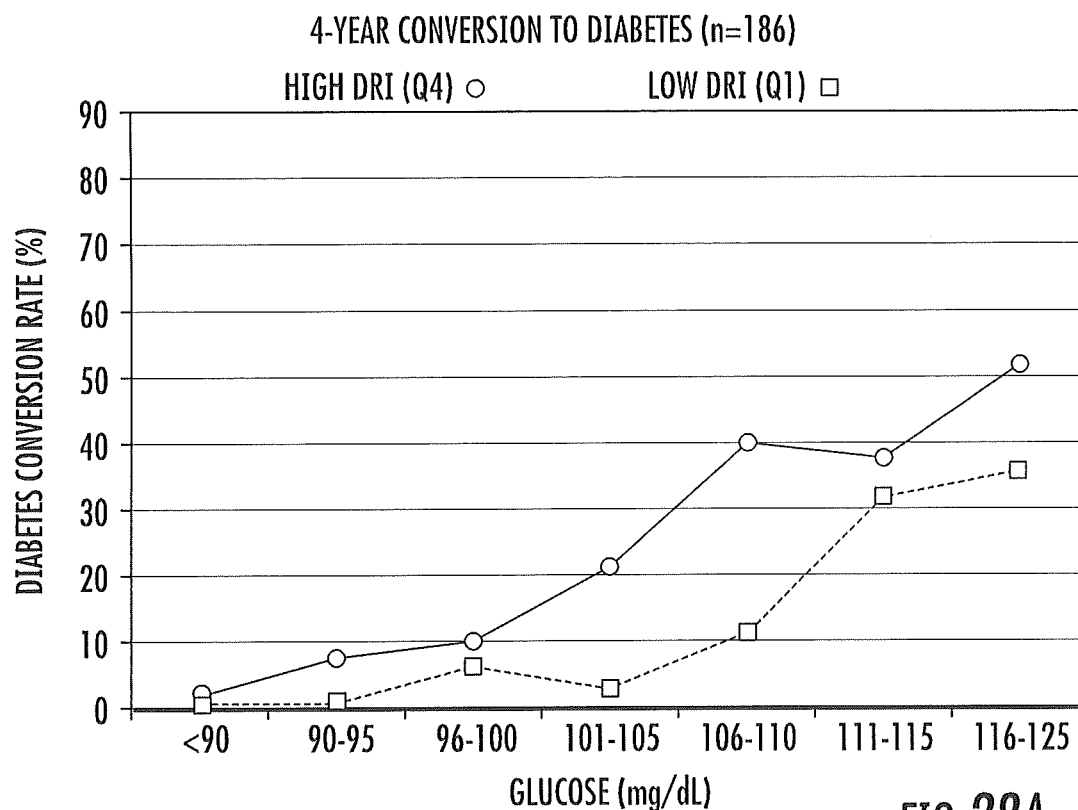


FIG. 28A

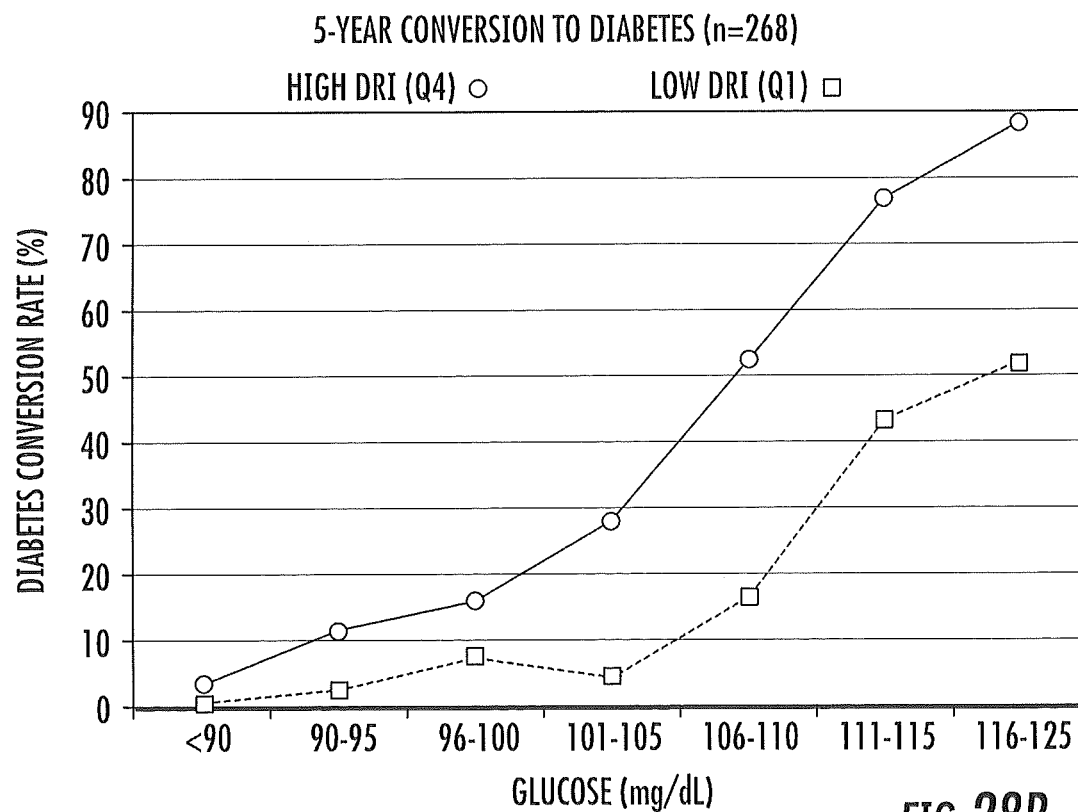


FIG. 28B

28/31

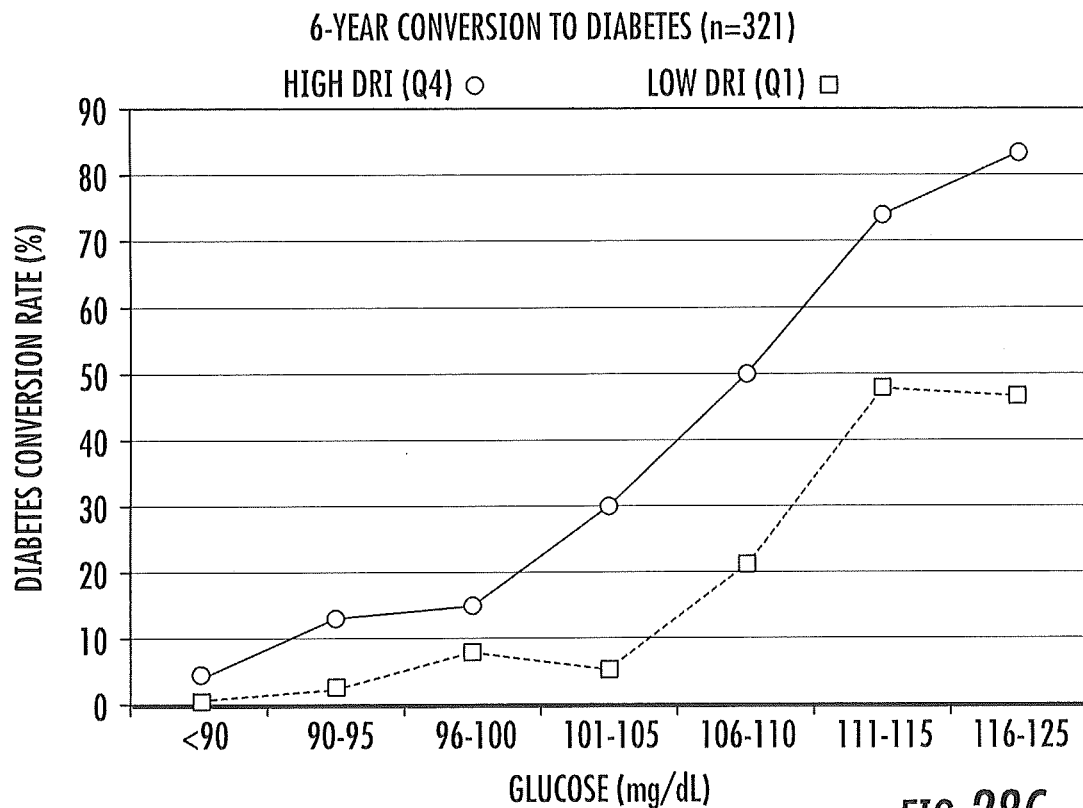


FIG. 28C

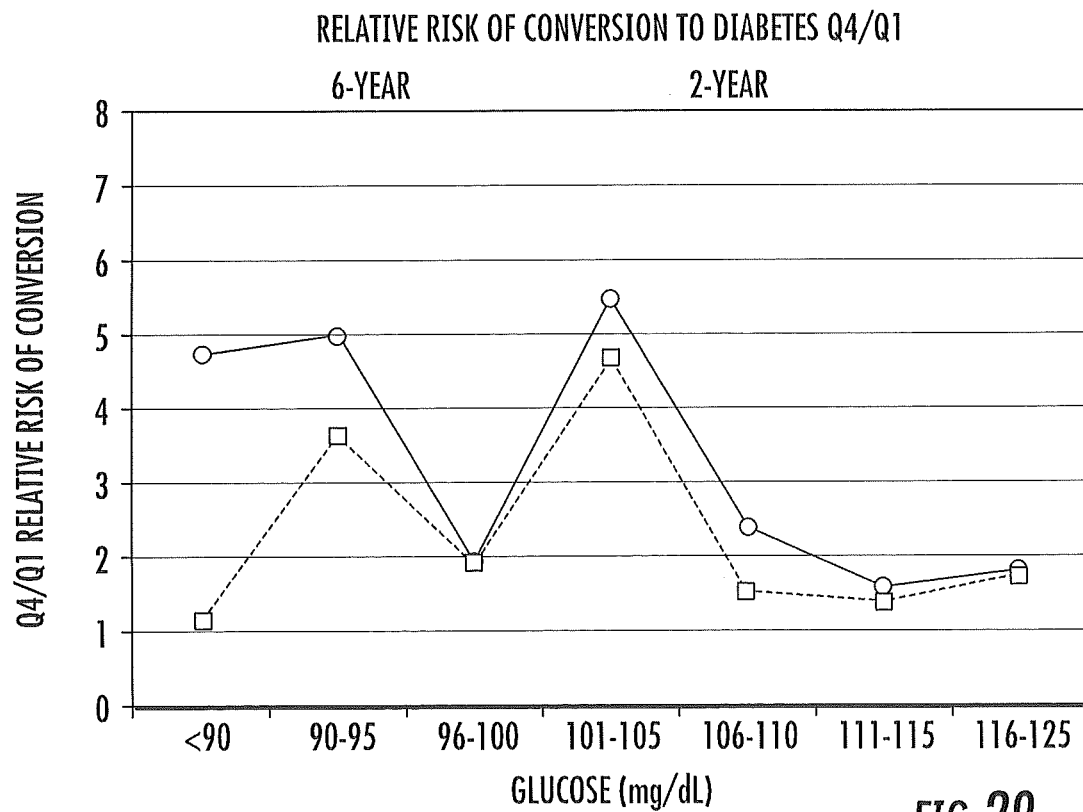


FIG. 29

29/31

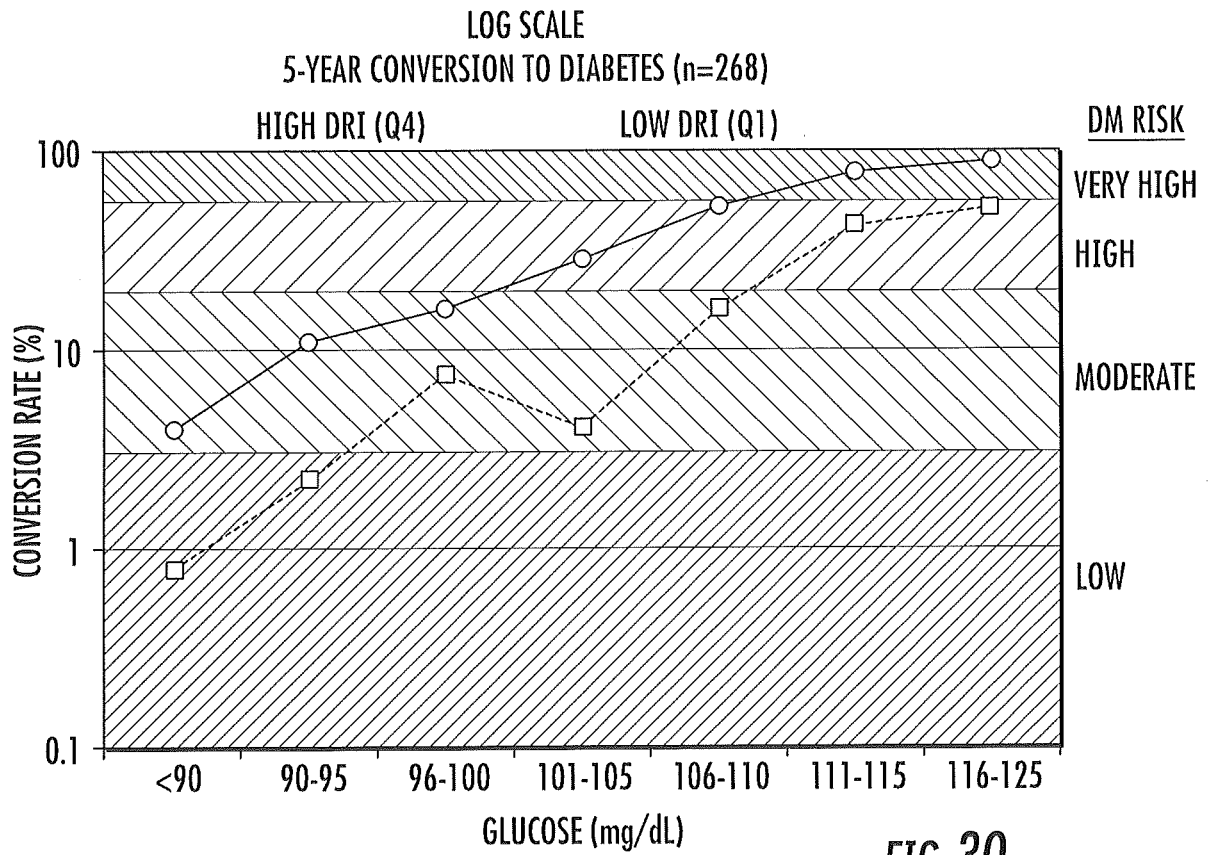


FIG. 30

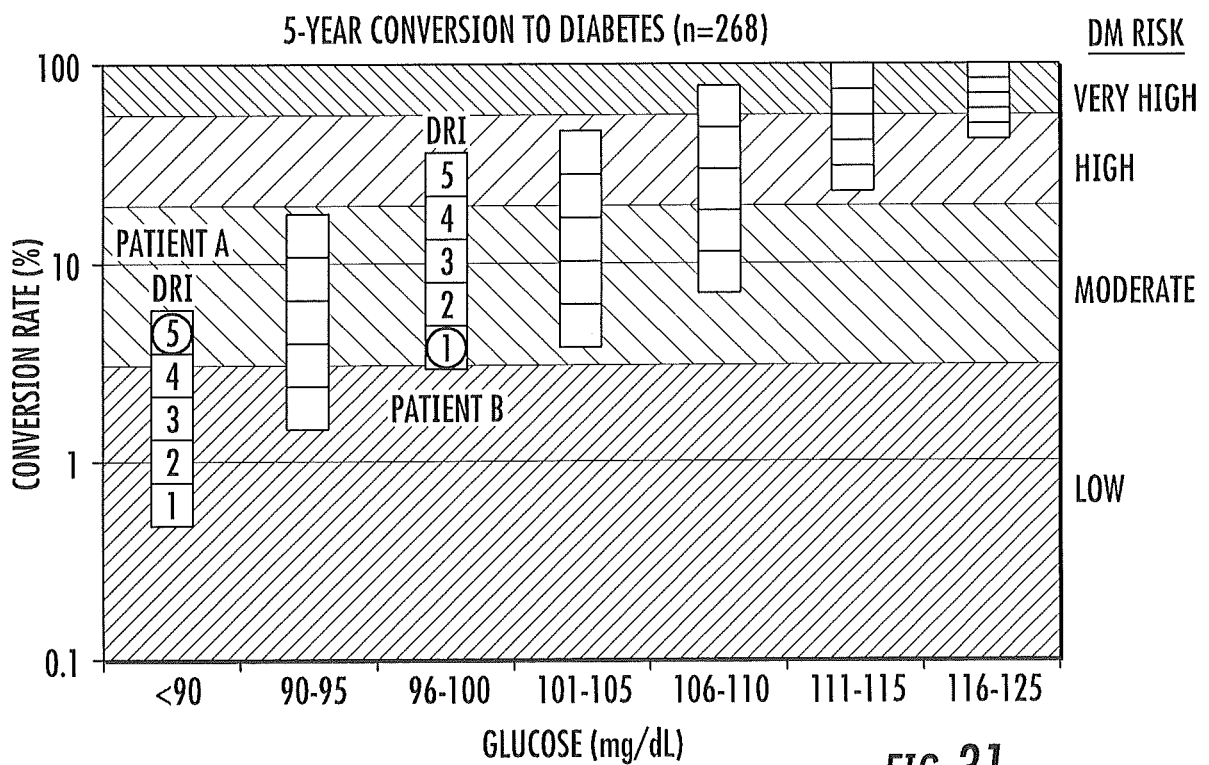


FIG. 31

30/31

DRIp IRAS GLUCOSE SUBGROUP-SPECIFIC QUINTILES														
GLUCOSE=<90 mg/dL				Q5/Q1	GLUCOSE=90-110 mg/dL				Q5/Q1	GLUCOSE>110 mg/dL				Q5/Q1
QUINTILES	N	NEW DIABETES	%		QUINTILES	N	NEW DIABETES	%		QUINTILES	N	NEW DIABETES	%	
1	47	0	1.0		1	122	7	5.7		1	27	4	14.8	
2	50	2	4.0		2	118	11	9.3		2	25	8	32.0	
3	49	1	2.0		3	122	15	12.3		3	28	9	32.1	
4	50	3	6.0		4	122	17	13.9		4	25	10	40.0	
5	49	3	6.1	6.1	5	121	29	24.0	4.2	5	27	15	55.6	3.8
Σ	245	9	3.7		Σ	605	79	13.1		Σ	132	46	34.8	
DRIp MESA GLUCOSE SUBGROUP-SPECIFIC QUINTILES														
GLUCOSE<90 mg/dL (1)				Q5/Q1	GLUCOSE 90-110 mg/dL (2)				Q5/Q1	GLUCOSE >110 mg/dL				Q5/Q1
QUINTILES	N	NEW DIABETES	%		QUINTILES	N	NEW DIABETES	%		QUINTILES	N	NEW DIABETES	%	
1	522	6	1.1		1	424	11	2.6		1	46	25	54.3	
2	553	4	0.7		2	395	22	5.6		2	46	21	45.7	
3	548	8	1.5		3	407	41	10.1		3	47	28	59.6	
4	549	20	3.6		4	403	44	10.9		4	46	32	69.6	
5	543	22	4.1	3.5	5	409	92	22.5	8.7	5	47	35	74.5	1.4
Σ	2715	60	2.2		Σ	2038	210	10.3		Σ	232	141	60.8	
DRIp MESA GLUCOSE SUBGROUP-SPECIFIC QUINTILES FROM MESA														
GLUCOSE=<90 mg/dL				Q5/Q1	GLUCOSE=90-110 mg/dL				Q5/Q1	GLUCOSE>110 mg/dL				Q5/Q1
QUINTILES	N	NEW DIABETES	%		QUINTILES	N	NEW DIABETES	%		QUINTILES	N	NEW DIABETES	%	
1	23	0	1.0		1	77	5	6.5		1	28	4	14.3	
2	24	0	0.0		2	74	4	5.4		2	21	8	38.1	
3	44	2	4.5		3	105	11	10.5		3	25	9	36.0	
4	55	1	1.8		4	118	13	11.0		4	27	10	37.0	
5	99	6	6.1	6.1	5	231	46	19.9	3.1	5	31	15	48.4	3.4
Σ	245	9	3.7		Σ	605	79	13.1		Σ	132	46	34.8	

FIG. 32

31/31

DRI-NMR IRAS				GLUCOSE SUBGROUP-SPECIFIC QUINTILES										
GLUCOSE= $\leq$ 90 mg/dL				Q5/Q1	GLUCOSE=90-110 mg/dL				Q5/Q1	GLUCOSE $>$ 110 mg/dL				Q5/Q1
QUINTILES	N	NEW DIABETES	%		QUINTILES	N	NEW DIABETES	%		QUINTILES	N	NEW DIABETES	%	
1	59	1	1.7		1	120	10	8.3		1	26	6	23.1	
2	51	1	2.0		2	122	13	10.7		2	27	7	25.9	
3	52	3	5.8		3	120	14	11.7		3	27	8	29.6	
4	46	1	2.2		4	122	23	18.9		4	26	11	42.3	
5	37	3	8.1	4.8	5	121	19	15.7	1.9	5	26	14	53.8	2.3
Σ	245	9	3.7		Σ	605	79	13.1		Σ	132	46	34.8	

DRI-NMR MESA				GLUCOSE SUBGROUP-SPECIFIC QUINTILES										
GLUCOSE $<$ 90 mg/dL (1)				Q5/Q1	GLUCOSE 90-110 mg/dL				Q5/Q1	GLUCOSE $>$ 110 mg/dL				Q5/Q1
QUINTILES	N	NEW DIABETES	%		QUINTILES	N	NEW DIABETES	%		QUINTILES	N	NEW DIABETES	%	
1	546	6	1.1		1	405	13	3.2		1	46	26	56.5	
2	538	5	0.9		2	408	39	9.6		2	47	26	55.3	
3	546	11	2.0		3	411	37	9.0		3	47	29	61.7	
4	542	17	3.1		4	405	58	14.3		4	45	30	66.7	
5	543	21	3.9	3.5	5	409	63	15.4	4.8	5	47	30	63.8	1.1
Σ	2715	60	2.2		Σ	2038	210	10.3		Σ	232	141	60.8	

DRI-NMR IRAS				GLUCOSE SUBGROUP-SPECIFIC QUINTILES FROM MESA										
GLUCOSE= $\leq$ 90 mg/dL (1)				Q5/Q1	GLUCOSE=90-110 mg/dL (2)				Q5/Q1	GLUCOSE $>$ 110 mg/dL				Q5/Q1
QUINTILES	N	NEW DIABETES	%		QUINTILES	N	NEW DIABETES	%		QUINTILES	N	NEW DIABETES	%	
1	39	0	1.0		1	96	7	7.3		1	25	5	20.0	
2	28	1	3.6		2	96	8	8.3		2	27	8	29.6	
3	41	1	2.4		3	90	14	15.6		3	16	2	12.5	
4	61	4	6.6		4	140	19	13.6		4	23	10	43.5	
5	79	3	3.9	3.9	5	183	31	16.9	2.3	5	41	21	51.2	2.6
Σ	245	9	3.7		Σ	605	79	13.1		Σ	132	46	34.8	

FIG. 33