

Supplementary Table S1 – Codes

Liver blood tests and their values were identified from the CPRD “test” dataset using the following entity file codes: ALT = 155; AST = 156; ALP = 153; GGT = 172; Bilirubin = 158; Platelet count = 189.			
Type 2 diabetes			
C100112	Non-insulin dependent diabetes mellitus	C109200	Non-insulin-dependent diabetes mellitus with neuro comps
C107400	NIDDM with peripheral circulatory disorder	C109211	Type II diabetes mellitus with neurological complications
C109.00	Non-insulin dependent diabetes mellitus	C109212	Type 2 diabetes mellitus with neurological complications
C109.11	NIDDM - Non-insulin dependent diabetes mellitus	C109300	Non-insulin-dependent diabetes mellitus with multiple comps
C109.12	Type 2 diabetes mellitus	C109312	Type 2 diabetes mellitus with multiple complications
C109.13	Type II diabetes mellitus	C109400	Non-insulin dependent diabetes mellitus with ulcer
C109000	Non-insulin-dependent diabetes mellitus with renal comps	C109411	Type II diabetes mellitus with ulcer
C109011	Type II diabetes mellitus with renal complications	C109412	Type 2 diabetes mellitus with ulcer
C109012	Type 2 diabetes mellitus with renal complications	C109500	Non-insulin dependent diabetes mellitus with gangrene
C109100	Non-insulin-dependent diabetes mellitus with ophthalmic comps	C109511	Type II diabetes mellitus with gangrene
C109111	Type II diabetes mellitus with ophthalmic complications	C109512	Type 2 diabetes mellitus with gangrene
C109112	Type 2 diabetes mellitus with ophthalmic complications	C109600	Non-insulin-dependent diabetes mellitus with retinopathy
Obesity = BMI>30. Values obtained from entity file: weight =13 and height = 14. Calculate BMI for every available weight measurement (using single height measurement). If BMI > 30 at any stage up to end of follow-up for individual patient then include in Obesity population. Index date is first occurrence of BMI >30.			
Cirrhosis: Identified from READ codes/terms			
7609	Open operations on oesophageal varices	J612.12	Laennec's cirrhosis
7609300	Local ligation of oesophageal varices	J615.00	Cirrhosis - non alcoholic
7609400	Open injection sclerotherapy to oesophageal varices	J615.11	Portal cirrhosis
7609y11	Tanner devascularisation for bleeding varices	J615100	Multilobular portal cirrhosis
7609z00	Open operation on oesophageal varices NOS	J615300	Diffuse nodular cirrhosis
760C300	Fibreoptic endoscopic injection sclerotherapy oesoph varices	J615400	Fatty portal cirrhosis
760C500	Fibreoptic endoscopic banding of oesophageal varices	J615500	Hypertrophic portal cirrhosis
760F300	Rigid oesophagoscopy injection sclerotherapy oesoph varices	J615600	Capsular portal cirrhosis
760F400	Rigid oesophagoscopy banding of oesophageal varices	J615700	Cardiac portal cirrhosis
761D800	Fibreopt endoscop rubber band ligation of upper GIT varices	J615800	Juvenile portal cirrhosis
C310400	Glycogenosis with hepatic cirrhosis	J615812	Indian childhood cirrhosis

C350012	Pigmentary cirrhosis of liver	J615C00	Xanthomatous portal cirrhosis
G85..11	Oesophageal varices	J615D00	Bacterial portal cirrhosis
G850.00	Oesophageal varices with bleeding	J615H00	Infectious cirrhosis NOS
G851.00	Oesophageal varices without bleeding	J615y00	Portal cirrhosis unspecified
G852.00	Oesophageal varices in diseases EC	J615z00	Non-alcoholic cirrhosis NOS
G852000	Oesophageal varices with bleeding in diseases EC	J615z11	Macronodular cirrhosis of liver
G852100	Oesophageal varices without bleeding in diseases EC	J615z12	Cryptogenic cirrhosis of liver
G852200	Oesophageal varices in cirrhosis of the liver	J615z13	Cirrhosis of liver NOS
G852300	Oesophageal varices in alcoholic cirrhosis of the liver	J616.00	Biliary cirrhosis
G852z00	Oesophageal varices in diseases EC NOS	J616100	Secondary biliary cirrhosis
G857.00	Gastric varices	J616200	Biliary cirrhosis of children
G858.00	Oesophageal varices NOS	J616z00	Biliary cirrhosis NOS
J61..00	Cirrhosis and chronic liver disease	J623.00	Portal hypertension
J612.00	Alcoholic cirrhosis of liver	J635600	Toxic liver disease with fibrosis and cirrhosis of liver
J612.11	Florid cirrhosis	Jyu7100	[X]Other and unspecified cirrhosis of liver
Alcohol excess: Identified from units per week from entity file (entity=5) and READ codes/terms			
136K.00	Alcohol intake above recommended sensible limits	E231.00	Chronic alcoholism
136S.00	Hazardous alcohol use	E231z00	Chronic alcoholism NOS
136T.00	Harmful alcohol use	E23z.00	Alcohol dependence syndrome NOS
136W.00	Alcohol misuse	E250.00	Nondependent alcohol abuse
8H7p.00	Referral to community alcohol team	E250000	Nondependent alcohol abuse, unspecified
9NN2.00	Under care of community alcohol team	E250200	Nondependent alcohol abuse, episodic
9k1..00	Alcohol misuse - enhanced services administration	E250z00	Nondependent alcohol abuse NOS
9k1A.00	Brief intervention for excessive alcohol consumption completed	Eu10211	[X]Alcohol addiction
E23..00	Alcohol dependence syndrome	Eu10212	[X]Chronic alcoholism
E23..11	Alcoholism	ZV11300	[V]Personal history of alcoholism
E23..12	Alcohol problem drinking		

Supplementary Table S2 – Total numbers of tests measured and individuals being tested

	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
ALT													
Total tests	145,762	182,250	220,863	264,573	299,956	336,059	349,857	355,185	377,633	379,820	336,022	274,827	199,196
Total people tested	101,485	126,562	152,516	183,196	206,761	228,380	239,920	246,920	261,544	264,206	233,037	193,654	141,885
AST													
Total tests	62,414	69689	72,998	69218	75,502	81218	78,629	79997	71,305	53,714	44,064	36,542	18,363
Total people tested	44,294	49158	51,781	48791	53,406	56756	56,085	57243	50,856	39,178	31,411	26,275	13,075
ALP													
Total tests	199,350	241693	288,224	326253	368,076	411994	426,350	442311	461,329	454,319	405,753	332,655	236,886
Total people tested	136,121	163894	192,150	218956	245,608	269713	280,957	292771	302,822	296,931	261,378	215,265	156,549
GGT													
Total tests	78,572	92452	102,634	111127	119,522	127386	132,905	127210	116,707	102,085	74,190	61,516	40,953
Total people tested	54,346	64692	71,192	78118	84,354	88723	93,147	90618	82,859	75,125	55,022	45,726	30,507
Bilirubin													
Total tests	192,632	231683	275,631	311066	350,373	388612	399,189	411125	426,237	412,887	366,861	299,687	215,528
Total people tested	134,046	160842	189,233	215296	241,713	264757	274,782	286590	295,722	288,212	254,867	210,081	152,916
Platelet count													
Total tests	269,019	318699	368,616	419187	475,732	524655	540,431	555732	589,239	557,555	495,158	389,745	279,714
Total people tested	158,987	185336	211,828	238400	265,257	289243	300,868	314311	324,861	315,432	279,168	230,590	167,506

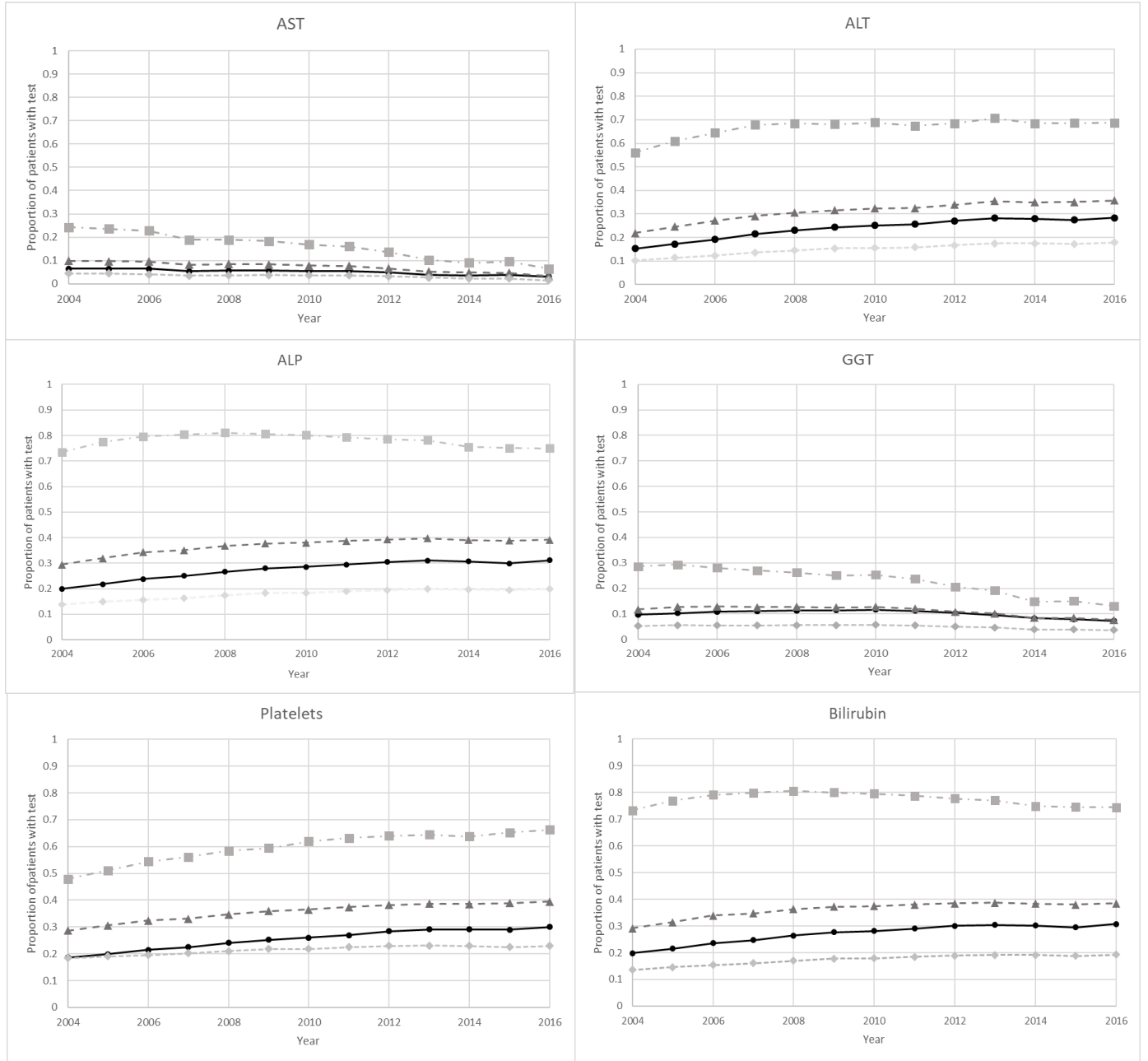
Supplementary Table S3 Prevalence of liver blood markers over time

	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
ALT													
<i>All</i>	13.0%	14.7%	16.1%	17.8%	19.0%	20.0%	20.5%	20.9%	22.0%	23.2%	23.0%	23.1%	23.7%
	101,485	126,562	152,516	183,196	206,761	228,380	239,920	246,920	261,544	264,206	233,037	193,654	141,885
<i>No risk factor</i>	10.2%	11.5%	12.3%	13.7%	14.6%	15.4%	15.6%	15.9%	16.7%	17.5%	17.4%	17.3%	17.9%
	58,099	71,085	82,630	97,925	109,206	119,415	122,910	125,077	131,327	131,491	115,211	93,323	69,323
<i>Alcohol excess</i>	15.3%	17.2%	19.2%	21.5%	23.1%	24.4%	25.1%	25.6%	27.1%	28.3%	28.0%	27.4%	28.3%
	15,571	19,838	24,616	30,304	34,840	38,992	41,558	42,907	45,955	46,207	41,346	34,669	23,270
<i>Obesity</i>	21.9%	24.6%	27.2%	29.2%	30.6%	31.6%	32.4%	32.5%	33.9%	35.4%	35.0%	35.1%	35.7%
	25,460	33,357	42,787	53,140	61,862	70,159	76,530	80,517	86,275	88,493	79,136	68,224	50,029
<i>Type 2 diabetes</i>	56.1%	61.0%	64.4%	67.9%	68.4%	68.1%	68.9%	67.4%	68.5%	70.7%	68.4%	68.6%	68.8%
	10,271	13,741	17,680	21,964	24,670	27,140	29,564	31,100	33,335	34,909	31,408	27,066	20,317
<i>All 3 risk factors</i>	59.1%	63.9%	68.4%	71.7%	72.4%	71.9%	71.5%	70.7%	70.3%	73.0%	71.3%	70.2%	71.1%
	874	1247	1685	2186	2613	3035	3430	3769	3983	4260	3931	3510	2436
AST													
<i>All</i>	5.7%	5.7%	5.5%	4.7%	4.9%	5.0%	4.8%	4.8%	4.3%	3.4%	3.1%	3.1%	2.2%
	44,294	49,158	51,781	48,791	53,406	56,756	56,085	57,243	50,856	39,178	31,411	26,275	13,075
<i>No risk factor</i>	4.4%	4.5%	4.1%	3.6%	3.7%	3.7%	3.6%	3.7%	3.3%	2.6%	2.3%	2.3%	1.6%
	25,237	27,674	27,556	25,603	27,614	28,920	28,504	29,130	25,902	19,882	15,406	12,526	6,017
<i>Alcohol excess</i>	6.5%	6.5%	6.5%	5.5%	5.6%	5.7%	5.5%	5.5%	4.8%	3.9%	3.6%	3.8%	3.0%
	6,672	7,446	8,311	7,708	8,497	9,129	9,123	9,214	8,206	6,298	5,368	4,791	2,503
<i>Obesity</i>	9.8%	9.7%	9.6%	8.2%	8.4%	8.3%	7.8%	7.6%	6.6%	5.3%	4.8%	4.8%	3.4%
	11,411	13,137	15,047	14,942	17,073	18,511	18,354	18,929	16,709	13,124	10,921	9,327	4,740
<i>Type 2 diabetes</i>	24.3%	23.6%	22.8%	18.9%	18.9%	18.4%	16.8%	16.0%	13.6%	10.3%	9.1%	9.6%	6.5%
	4,444	5,309	6,257	6,104	6,808	7,318	7,228	7,387	6,599	5,099	4,155	3,780	1,919
<i>All 3 risk factors</i>	24.9%	24.4%	22.6%	18.9%	18.7%	18.0%	16.5%	15.3%	12.7%	9.9%	9.2%	9.6%	7.4%
	369	477	557	577	676	759	793	813	721	576	506	478	252
ALP													

<i>All</i>	17.4%	19.0%	20.3%	21.3%	22.6%	23.7%	24.0%	24.8%	25.5%	26.0%	25.8%	25.6%	26.2%
	136,121	163,894	192,150	218,956	245,608	269,713	280,957	292,771	302,822	296,931	261,378	215,265	156,549
<i>No risk factor</i>	13.8%	14.9%	15.6%	16.4%	17.4%	18.2%	18.3%	19.0%	19.5%	19.9%	19.7%	19.4%	19.9%
	78,382	92,690	104,627	117,407	129,995	141,235	144,684	149,282	153,272	149,168	130,327	104,727	76,926
<i>Alcohol excess</i>	20.0%	21.7%	23.8%	25.0%	26.6%	27.9%	28.6%	29.4%	30.5%	31.0%	30.7%	29.9%	31.1%
	20,355	25,039	30,447	35,275	40,123	44,632	47,212	49,230	51,624	50,602	45,304	37,836	25,565
<i>Obesity</i>	29.5%	31.9%	34.3%	35.1%	36.8%	37.7%	38.1%	38.7%	39.2%	39.7%	39.1%	38.8%	39.2%
	34,314	43,222	53,982	63,964	74,331	83,756	89,904	95,755	99,898	99,094	88,395	75,373	54,922
<i>Type 2 diabetes</i>	73.5%	77.4%	79.6%	80.4%	81.0%	80.6%	80.2%	79.3%	78.6%	78.2%	75.5%	75.1%	75.0%
	13,458	17,429	21,845	26,018	29,210	32,115	34,420	36,568	38,245	38,590	34,647	29,619	22,161
<i>All 3 risk factors</i>	75.0%	79.1%	82.1%	82.0%	82.7%	81.9%	80.8%	80.8%	78.9%	78.7%	77.1%	75.5%	77.2%
	1,110	1,544	2,021	2,501	2,986	3,455	3,876	4,305	4,471	4,588	4,251	3,774	2,645
GGT													
<i>All</i>	7.0%	7.5%	7.5%	7.6%	7.8%	7.8%	8.0%	7.7%	7.0%	6.6%	5.4%	5.4%	5.1%
	54,346	64,692	71,192	78,118	84,354	88,723	93,147	90,618	82,859	75,125	55,022	45,726	30,507
<i>No risk factor</i>	5.3%	5.6%	5.5%	5.5%	5.6%	5.6%	5.7%	5.5%	5.0%	4.7%	3.9%	3.9%	3.7%
	29,868	34,865	36,661	39,595	42,214	43,632	45,103	43,616	39,378	35,625	25,434	20,846	14,408
<i>Alcohol excess</i>	9.7%	10.3%	10.8%	11.0%	11.3%	11.5%	11.7%	11.2%	10.4%	9.6%	8.3%	7.9%	7.3%
	9,837	11,909	13,845	15,572	17,021	18,307	19,323	18,790	17,571	15,738	12,271	9,922	5,971
<i>Obesity</i>	11.8%	12.8%	12.9%	12.6%	12.8%	12.6%	12.8%	12.1%	10.9%	10.2%	8.4%	8.5%	7.7%
	13,754	17,296	20,350	23,024	25,877	27,954	30,300	29,929	27,680	25,385	19,030	16,469	10,731
<i>Type 2 diabetes</i>	28.6%	29.3%	28.0%	27.1%	26.2%	25.1%	25.3%	23.7%	20.7%	19.2%	14.8%	15.1%	13.1%
	5,232	6,601	7,693	8,757	9,456	10,007	10,855	10,946	10,061	9,484	6,796	5,942	3,879
<i>All 3 risk factors</i>	32.2%	33.8%	33.0%	32.2%	31.3%	31.1%	30.1%	29.4%	24.6%	22.6%	18.3%	17.8%	14.8%
	476	659	812	982	1,131	1,314	1,443	1,568	1,394	1,319	1,009	891	507
Bilirubin													
<i>All</i>	17.2%	18.6%	20.0%	20.9%	22.2%	23.2%	23.5%	24.3%	24.9%	25.3%	25.2%	25.0%	25.6%
	134,046	160,842	189,233	215,296	241,713	264,757	274,782	286,590	295,722	288,212	254,867	210,081	152,916
	13.5%	14.6%	15.3%	16.1%	17.0%	17.8%	17.8%	18.4%	18.9%	19.2%	19.1%	18.8%	19.3%

<i>No risk factor</i>	76,925	90,589	102,695	114,978	127,452	137,983	140,694	145,318	148,912	143,914	126,200	101,520	74,600
<i>Alcohol excess</i>	19.8% 20,174	21.5% 24,766	23.5% 30,144	24.7% 34,890	26.4% 39,753	27.6% 44,116	28.2% 46,549	29.0% 48,609	30.0% 50,790	30.3% 49,536	30.2% 44,537	29.4% 37,217	30.7% 25,195
<i>Obesity</i>	29.1% 33,896	31.4% 42,574	33.9% 53,306	34.7% 63,125	36.3% 73,377	37.2% 82,584	37.4% 88,397	38.0% 94,097	38.5% 97,916	38.7% 96,601	38.3% 86,706	38.0% 73,942	38.5% 53,945
<i>Type 2 diabetes</i>	73.2% 13,402	76.9% 17,306	79.1% 21,709	79.9% 25,850	80.5% 29,030	80.0% 31,878	79.5% 34,108	78.7% 36,294	77.7% 37,812	77.0% 38,009	74.8% 34,346	74.5% 29,378	74.4% 21,978
<i>All 3 risk factors</i>	74.8% 1,107	78.7% 1,536	81.6% 2,010	81.8% 2,494	82.4% 2,976	81.6% 3,443	80.5% 3,862	80.4% 4,284	78.2% 4,430	77.9% 4,544	76.6% 4,222	75.0% 3,749	76.8% 2,629
Platelets													
<i>All</i>	20.3% 158,987	21.5% 185,336	22.4% 211,828	23.2% 238,400	24.4% 265,257	25.4% 289,243	25.7% 300,868	26.6% 314,311	27.4% 324,861	27.6% 315,432	27.6% 279,168	27.5% 230,590	28.0% 167,506
<i>No risk factor</i>	18.3% 104,008	19.1% 118,472	19.5% 130,674	20.1% 144,262	21.0% 157,524	21.8% 168,847	21.8% 172,317	22.5% 177,447	23.0% 180,888	23.1% 173,265	22.9% 151,378	22.4% 121,000	22.9% 88,638
<i>Alcohol excess</i>	18.6% 18,994	19.9% 22,933	21.4% 27,424	22.5% 31,684	24.0% 36,207	25.2% 40,327	26.0% 42,991	27.0% 45,170	28.4% 48,143	29.0% 47,396	29.1% 42,957	29.0% 36,654	30.0% 24,657
<i>Obesity</i>	28.7% 33,393	30.6% 41,452	32.4% 50,954	33.1% 60,244	34.7% 70,172	35.9% 79,767	36.5% 86,087	37.5% 92,765	38.3% 97,383	38.6% 96,496	38.6% 87,227	38.9% 75,562	39.4% 55,216
<i>Type 2 diabetes</i>	47.9% 8,764	51.1% 11,511	54.4% 14,932	56.1% 18,153	58.3% 21,031	59.5% 23,689	61.9% 26,553	63.2% 29,146	64.0% 31,107	64.4% 31,793	63.7% 29,233	65.3% 25,752	66.3% 19,593
<i>All 3 risk factors</i>	43.9% 650	48.6% 949	51.9% 1,278	52.9% 1,614	56.0% 2,020	56.9% 2,403	59.1% 2,835	61.2% 3,261	61.4% 3,477	63.0% 3,674	62.7% 3,455	64.2% 3,210	67.8% 2,323

Supplementary Figure S1 Prevalence of liver marker testing over time by the subgroups: no liver risk factors, Type 2 diabetes, excess alcohol consumption and obesity



—●— Alcohol -▲- Obese -■- Type 2 diabetes -◇- No risk factors