Supplemental Material:

1. **Table S1.** Comparison of Participants Characteristics between population with and without complete pre-treated LDL data in both Familial Hypercholesterolemia Phenotype and Normal LDL-C population groups.

2. **Table S2.** Incidence rate (1000 person-years) and hazard ratio of atherosclerotic cardiovascular disease by age in primary prevention. Complete-case analysis.

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6. **Figure S1.** Incidence rate (per 1000 person-years) of CHD in primary prevention in FH-P vs normolipidemic population based on the presence of number of cardiovascular risk factors

7. **Figure S2.** Incidence rate (per 1000 person-years) of CHD in secondary prevention in FH-P vs normolipidemic population based on the presence of number of cardiovascular risk factors and clinical associated characteristics

8. ICD-9 and ICD-10 codes included in the definition of ASCVD (coronary heart disease, ischemic stroke and peripheral artery disease)

Table S1. Comparison of Participants Characteristics between population with and without complete pre-treated LDL data in both Familial Hypercholesterolemia Phenotype and Normal LDL-C population groups.

Variable	Normal LDL-C population (<115 mg/dL)			Familial Hypercholesterolemia Phenotype		
	Complete-case	Imputed-case	p-value	Complete-case	Imputed-case	p-value
N	490,959	23,218		2,652	10,171	
Age, mean (SD)	49.3 (19.9)	71.2 (10.9)	<0.0001	51.7 (15.5)	64.4 (11.5)	<0.0001
Sex (male), %	42.2%	56.7%	<0.0001	44.3%	44.9%	0.6126
Receiving lipid lowering therapy, %	2.3%	100.0%	-	46.8%	100.0%	-
Diabetes mellitus, %	15.1%	50.9%	<0.0001	11.5%	27.7%	<0.0001
Hypertension, %	35.9%	89.7%	<0.0001	39.6%	73.3%	<0.0001
Current smoker, %	31.1%	37.5%	<0.0001	41.7%	33.6%	<0.0001
Body mass index, mean (SD)	27.6 (5.6)	29.5 (4.8)	<0.0001	28.1 (4.8)	29.2 (4.6)	<0.0001
Obesity, %	21.8%	40.5%	<0.0001	23.4%	34.5%	<0.0001
TC, mg/dL, mean (SD)	169.5 (26.0)	162.7 (34.4)	<0.0001	314.6 (73.3)	236.0 (43.2)	<0.0001
LDL-C, mg/dL, mean (SD)	91.8 (16.9)	81.9 (25.3)	<0.0001	236.3 (65.8)	155.8 (37.2)	<0.0001
HDL-C, mg/dL, mean (SD)	55.8 (16.4)	51.1 (15.5)	<0.0001	54.8 (14.4)	55.8 (13.7)	0.0049
TG, mg/dL, mean (SD)	111.1 (73.4)	143.1 (95.2)	<0.0001	162.3 (106.5)	146.0 (81.2)	<0.0001
Creatinine, mg/dL, mean (SD)	0.9 (0.4)	1.0 (0.6)	<0.0001	0.9 (0.3)	0.9 (0.3)	0.0041
HBA1c, mean (SD)	5.8 (1.5)	6.4 (1.5)	<0.0001	6.0 (2.0)	6.1 (1.5)	0.5010

SD: standard deviation; BMI: Body Mass Index; TC: Total Cholesterol; LDL-C: Low-density lipoprotein cholesterol; HDL-C: High-density lipoprotein cholesterol; TG: triglycerides; HbA1C: Glycosylated haemoglobin.

Table S2. Incidence rate (1000 person-years) and hazard ratio of atherosclerotic cardiovascular disease by age in primary prevention. Complete-case analysis.

Age Groups	Normal LDL-C population (<115 mg/dL)			Familial Hypercholesterolemia Phenotype			
	Number (n)	Events (n)	IR (1000 p-y) 95%CI	Number (n)	Events (n)	IR (1000 p-y) 95%CI	HR 95%CI
All	459,934	14,574	6.6 (6.5-6.7)	2,489	132	11.2 (9.3-13.4)	2.11 (1.76-2.53)
0-35	141,845	142	0.2 (0.2-0.2)	433	5	2.3 (0.9-5.8)	9.20 (3.59-23.53)
35-45	91,022	476	1.1 (1.0-1.2)	473	17	7.3 (4.4-12.0)	4.69 (2.81-7.83)
45-55	69,489	1,205	3.5 (3.3-3.7)	532	29	11.4 (7.7-16.7)	2.59 (1.75-3.82)
55-65	54,442	2,433	9.3 (8.9-9.7)	586	39	14.1 (10.1-19.6)	1.83 (1.31-2.55)
65-75	46,720	3,779	17.5 (16.9-18.1)	282	20	15.6 (9.8-24.9)	1.13 (0.71-1.80)
75-85	40,631	4,689	27.4 (26.6-28.2)	158	19	29.2 (18.2-46.8)	1.36 (0.85-2.19)
>85	15,785	1,850	35.6 (33.9-37.3)	26	3	31.7 (8.4-120.2)	0.98 (0.26-3.69)

LDL-C: Low-density Lipoprotein Cholesterol; IR 1000 p/y: Incident Rate persons-years; CI: Confidence Interval; HR: Hazard Ratio.

Table S3. Incidence rate (1000 person-years) and hazard ratio of atherosclerotic cardiovascular disease by age in secondary prevention. Complete-case analysis.

Age Groups	Normal LDL-C population (<115 mg/dL)			Familial Hypercholesterolemia Phenotype			
	Number (n)	Events (n)	IR (1000 p-y) 95%CI	Number (n)	Events (n)	IR (1000 p-y) 95%CI	HR 95%CI
All	31,025	9,152	85.6 (83.8-87.5)	163	57	100.8 (76.6-132.8)	1.42 (1.07-1.88)
0-35	253	20	16.8 (10.6-26.7)	3	2	342.9 (80.1-1466.9)	25.48 (4.47-145.33)
35-45	616	111	40.8 (33.6-49.6)	6	3	133.5 (35.8-497.4)	2.85 (0.74-11.01)
45-55	1,800	464	62.7 (57.0-69.0)	23	8	90.9 (43.6-189.2)	1.26 (0.60-2.66)
55-65	4,228	1,202	71.1 (67.0-75.4)	45	16	100.7 (59.8-169.7)	1.61 (0.94-2.75)
65-75	7,169	2,259	83.6 (80.0-87.3)	38	12	80.5 (44.2-146.6)	1.07 (0.59-1.95)
75-85	10,961	3,544	98.0 (94.6-101.4)	36	12	109.3 (58.1-205.6)	1.33 (0.71-2.50)
>85	5,998	1,552	100.2 (95.1-105.6)	13	5	122.4 (44.9-333.4)	1.45 (0.53-3.96)

LDL-C: Low-density Lipoprotein Cholesterol; IR 1000 p/y: Incident Rate persons-years; CI: Confidence Interval; HR: Hazard Ratio.

Table S4. Incidence rate (1000 person/years) and hazard ratio of coronary heart disease by age in primary prevention

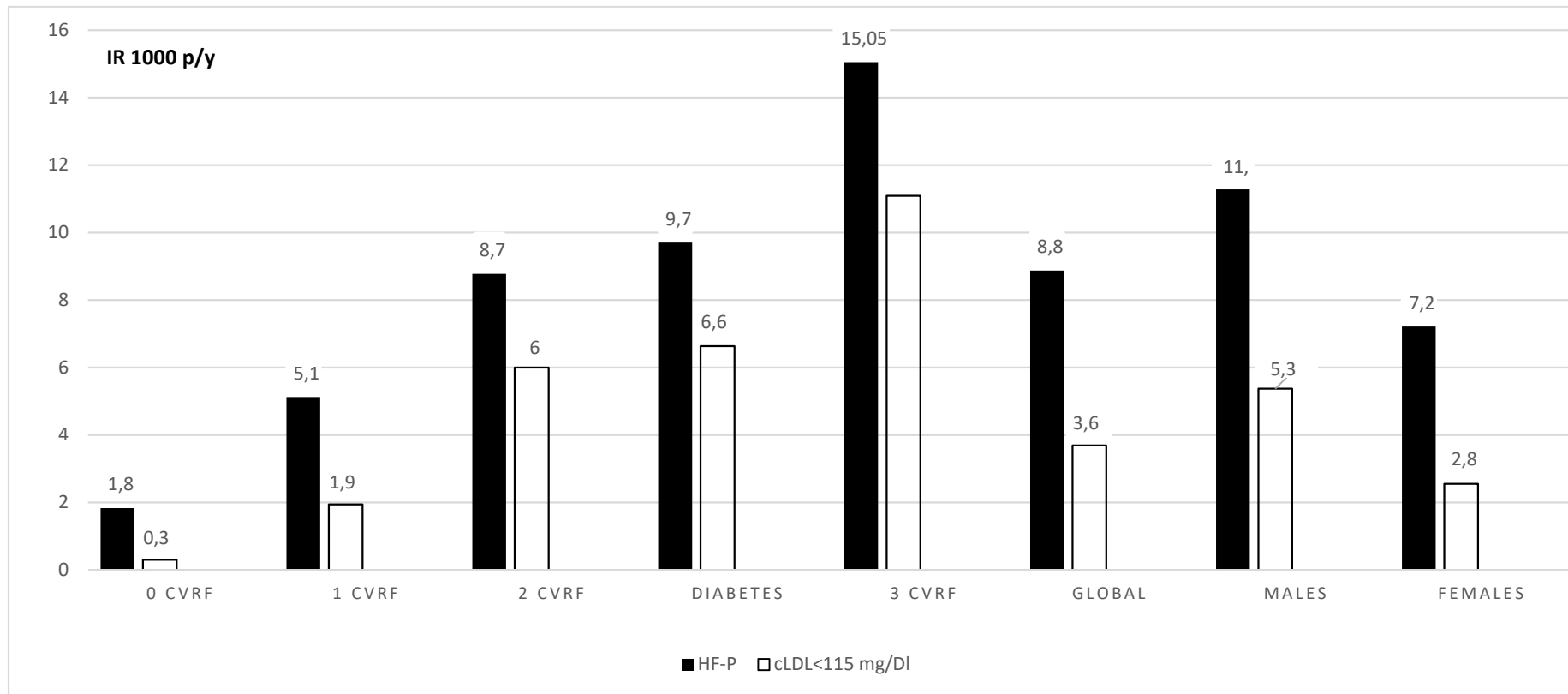| Age Groups	Normal LDL-C population (<115 mg/dL)			Familial Hypercholesterolemia Phenotype			
	Number (n)	Events (n)	IR (1000 p/y) 95%CI	Number (n)	Events (n)	IR (1000 p/y) IC 95	HR IC 95
All	472,591	4,728	2.07	10,621	298	5.8	1.95 (0.65-2.28)
0-35	141,920	40	0.02 (0.01-0.03)	551	5	1.7 (0.7-4)	16.70 (6.66-41.85)
35-45	91,274	180	0.07(0.06-0.11)	833	19	4.5 (2.9-7.1)	5.74 (3.59-9.20)
45-55	70,331	466	0.3 (0.2-0.3)	1,652	28	3.4 (2.3-5.0)	1.81 (1.22-0.68)
55-65	56,835	894	0.9 (0.80-1.08)	3,241	89	5.6 (4.59-6.9)	1.85 (1.50-2.28)
65-75	50,897	1,284	1.9 (1.7-2.2)	2,713	90	6.8 (5.3-9.0)	1.46 (1.11-1.91)
75-85	44,604	1,397	3.2 (2.7-3.8)	1,441	57	8.5 (5.9-12.2)	1.30 (0.90-1.89)
>85	16,730	467	3.5 (2.5-4.9)	189	11	1.4 (7.1-29.3)	1.81 (0.89-3.68)

LDL-C: Low-density Lipoprotein Cholesterol; IR 1000 p/y: Incident Rate 1000 persons-years; CI: Confidence Interval; HR: Hazard Ratio

Table S5. Incidence rate (1000 person/years) and hazard ratio of coronary heart disease by age in secondary prevention

	Normal LDL-C population (<115 mg/dL)			Familial Hypercholesterolemia Phenotype			
Age Groups	Number (n)	Events (n)	IR (1000 p/y) 95%CI	Number (n)	Events (n)	IR (1000 p/y) IC 95	HR IC 95
All	41,585	4,579	28.2	2,202	322	34.5	1.29 (1.08-1.53)
0-35	262	8	6.3 (3.3-11.9)	8	2	74.5 (18.06-307.6)	5.98 (0.81-44.06)
35-45	697	65	19.9 (15.9-25.0)	36	8	54.2 (26.1-112.1)	1.97 (0.93-4.20)
45-55	2,329	278	26.5 (23.6-29.7)	214	41	44.2 (32.1-60.8)	1.55 (1.11-2.17)
55-65	5,898	687	26.1 (24.2-28.2)	581	80	30.8 (23.4-40.7)	1.22 (0.91-1.63)
65-75	10,340	1,236	26.4 (26.49-29.7)	718	101	32.5 (26.2-40.2)	1.25 (1.00-1.56)
75-85	14,965	1,765	32.3 (29.8-32.8)	544	76	34.8 (26.8-45.3)	1.19 (0.90-1.57)
>85	7,094	540	26.1 (24.09-28.3)	100	13	36.6 (20.1-66.2)	1.49 (0.80-2.76)

LDL-C: Low-density Lipoprotein Cholesterol; IR 1000 p/y: Incident Rate 1000 persons-years; CI: Confidence Interval; HR: Hazard Ratio
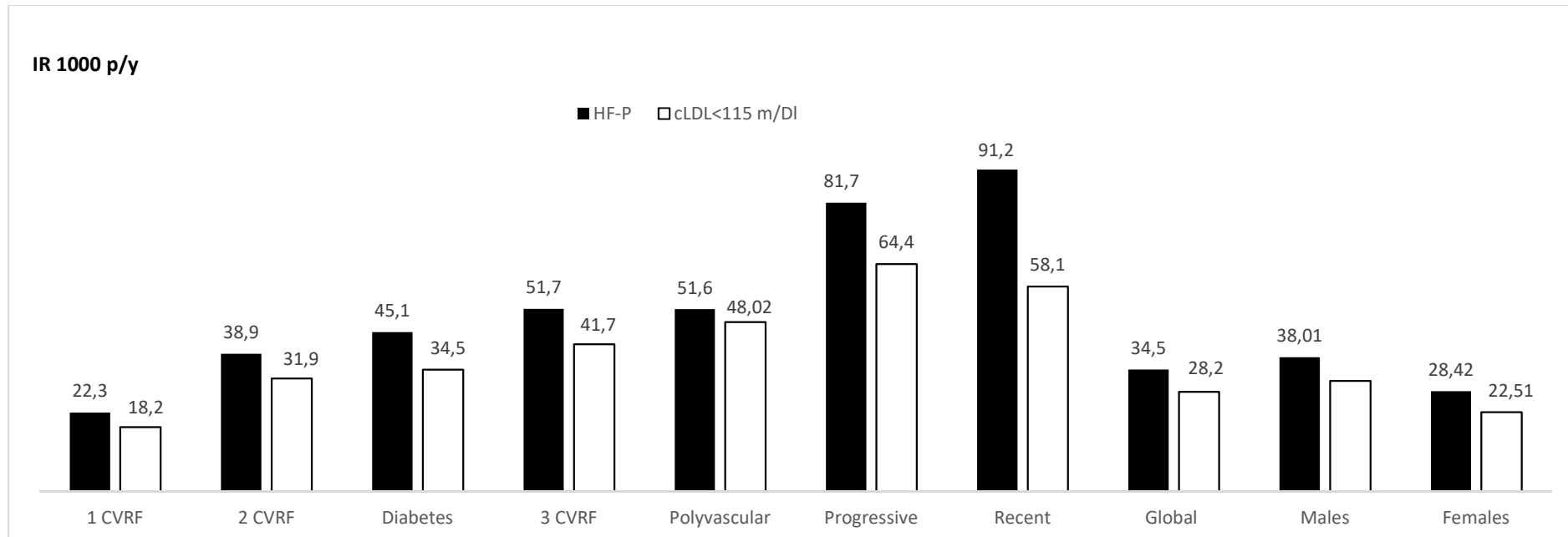
Fig S1. Incidence rate (per 1000 person-years) of CHD in primary prevention in FH-P vs normolipidemic population based on the presence of number of cardiovascular risk factors

CHD: Coronary Heart Disease; CVRF: Cardiovascular Risk Factor; FH-P: Familial Hypercholesterolemia Phenotype; LDL-C: Low-Density Lipoprotein Cholesterol

Fig S2. Incidence rate (per 1000 person-years) of CHD in secondary prevention in FH-P vs normolipidemic population based on the presence of number of cardiovascular risk factors and clinical associated characteristics

IR 1000 p/y

Legend: ■ HF-P □ cLDL<115 m/Dl

Category	HF-P	cLDL<115 m/Dl
1 CVRF	22,3	18,2
2 CVRF	38,9	31,9
Diabetes	45,1	34,5
3 CVRF	51,7	41,7
Polyvascular	51,6	48,02
Progressive	81,7	64,4
Recent	91,2	58,1
Global	34,5	28,2
Males	38,01	28,2
Females	28,42	22,51

CHD: Coronary Heart Disease; CVRF: Cardiovascular Risk Factor; HF-P: Familial Hypercholesterolemia; CLDL: Cholesterol-LDL

Coronary heart disease

ICD 9

410,
 4100, 41000, 41001, 41002,
 4101, 41010, 41011, 41012,
 4102, 41020, 41021, 41022,
 4103, 41030, 41031, 41032,
 4104, 41040, 41041, 41042,
 4105, 41050, 41051, 41052,
 4106, 41060, 41061, 41062,
 4107, 41070, 41071, 41072,
 4108, 41080, 41081, 41082,
 4109, 41090, 41091, 41092,
411, 4110, 4111, 4118, 41181, 41189
413, 4130, 4131, 4132, 4133, 4138, 4139
4140, 41400, 41401, 41402, 41403, 41404, 41405, 41406, 41407

ICD 10

I20, I20.0, I20.1, I20.8, I20.9
I21, I21.0, I21.1, I21.2, I21.3, I21.4, I21.9
I22, I22.0, I22.1, I22.8, I22.9
I23, I23.0, I23.1, I23.2, I23.3, I23.4, I23.5, I23.6, I23.8
I24, I24.0, I24.1, I24.8, I24.9

Ischemic stroke

ICD 9

433,
 4330, 43301, 4331, 43311, 4332, 43321, 4333, 43331, 4338, 43381, 4339, 43391
434,
 4340, 43401, 4341, 4342, 4349, 43491
438,
 4380,
 4381, 43810, 43811, 43812, 43813, 43814, 43819,
 4382, 43820, 43821, 43822,
 4383, 43830, 43831, 43832,
 4384, 43840, 43841, 43842,
 4385, 43850, 43851, 43852, 43853,
 4386,
 4387,
 4388, 43881, 43882, 43883, 43884, 43885, 43889,
 4389

ICD 10

I63, I63.0, I63.2, I63.3, I63.5, I63.6, I63.8, I63.9
I64
I65, I65.0, I65.1, I65.2, I65.3, I65.8, I65.9

Peripheral artery disease

ICD 9

44020, 44021, 44022, 44023, 44024, 44029,
4403, 44030, 44031, 44032,
4404
4439
44422, 44489

ICD 10

I70, I70.2, I70.8, I70.9
I73, I73.8, I73.9
I74.3