UKB CHD-Sex-Metabolite Project Update

Update for Raji & Kathy

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Summary

We gained access to download the UKBiobank NMR Metabolomics data on April 27, in addition to having access to the full cohort of UKBiobank data. Our first objective was to summarize some baseline characteristics in both the full UKB sample (N = 502,411) as well as the subset with available metabolomics (N = 121,716). We also summarized the occurrences of various cardiac-related outcomes after initial assessment in both the full sample and subset with metabolites. We stratified the summaries by sex (field 31) as well as included overall summaries.

Methods

I summarized number and percent of total for categorical variables such as smoking status, hysterectomy, menopause, and hormone replacement therapy (HRT) status. I calculated median and interquartile range (IQR) of several continuous measurements taken at first assessment visit (height, weight, body mass index (BMI), age at first assessment, body and trunk fat percentage, whole body impedance (estimated muscle mass), HbA1c, several blood pressure (BP) and pulse measurements (both automated and manual), and various bone mineral density (BMD) measures). Field code is included in the table in case definitions are needed for clarity.

By matching ICD10 codes (as described in the Said 2018 paper) in field 41270, I identified incident diagnosis of Hypertension, Type 2 Diabetes, Atrial Fibrilation, Stroke, and Coronary Artery Disease (CAD). I used the corresponding date of diagnoses (field 41280) and compared it to the date of initial assessment (field 53) to identify diagnoses that occurred after first assessment. Some subjects had more than one condition (e.g. both hypertension and diabetes), all distinct diagnoses are included. In cases where a subject had multiple dates for the same diagnosis (e.g. multiple dates recording hypertension), I used the first diagnosis date to compare to initial assessment at UKB assessment center.

I made an indicator variable "Has Metabolites" based on if subjects had any values entered in fields 23400-23948 to get the subset of 121,716 subjects with NMR metabolite measurements.

Next steps

The incident table should be thought of as a "lower bound" since it only includes diagnoses from the field of ICD10 codes, which were captured during in-patient hospital visits. We also need to look at the mortality, outpatient surgery, and self-reported diagnoses fields to capture a more precise estimate for the incidence of outcomes.

Next we will also need to do processing of the metabolite data itself before summarizing it and moving forward with analysis.

Questions

- What additional demographic/baseline assessment variables should we consider?
- What definitions of demographic/baseline assessment variables should we use (e.g. in cases where there are self-reported, automatic measurements, and manual entry, we should determine which measurement(s) to use)?
- Are there additional outcomes we should examine?

Tables

ICD10 Codes

The following ICD10 codes were used to identify outcomes of interest.

disease	ICD10
Coronary Artery Disease	I21-25, Z951, Z955
Atrial Fibrillation	I48
Stroke	I60, I61, I629, I63, I64, I678, I690, I693, G951, H341, H342, S066
Hypertension	I10-I13, I15, O10
Diabetes Mellitus Type 2	E10-E14

Summary of incidence of outcomes

The below table describes the number and percent of incident diagnoses (defined as ICD10 diagnosis that occurred after date of first assessment). "Samples with Metabolites" is defined as the subset of subjects with any entry in the NMR metabolite fields (23400-23948).

Left 3 columns are from the full dataset, right 3 columns are from the subset of subjects with available metabolite data.

Characteristic	**Overall**, N = 502,411	**Female**, N = 273,325	**Male**, N = 229,086	**Overall**, N = 121,716	**Female**, N = 65,774	**Male**, N = 55,942
CAD	41,565 (8.3%)	15,193 (5.6%)	26,372 (12%)	10,023 (8.2%)	3,646 (5.5%)	6,377 (11%)
Atrial Fibrillation	29,934 (6.0%)	11,442 (4.2%)	18,492 (8.1%)	7,284 (6.0%)	2,791 (4.2%)	4,493 (8.0%)
Stroke	11,827 (2.4%)	5,013 (1.8%)	6,814 (3.0%)	2,877 (2.4%)	1,200 (1.8%)	1,677 (3.0%)
Hypertension	111,578 (22%)	53,379 (20%)	58,199 (25%)	27,032 (22%)	12,796 (19%)	14,236 (25%)
Type 2 Diabetes	35,049 (7.0%)	14,593 (5.3%)	20,456 (8.9%)	8,408 (6.9%)	3,436 (5.2%)	4,972 (8.9%)

Summary of Baseline characteristics

The below table describes the distribution of various baseline characteristics and measurements, defined as measured at the first date of assessment.

Note that certain characteristics only have entry for subjects with Sex = Female (e.g. hysterectomy, menopause, and HRT status).

Also note that there were missing values for many of the variables. In the below table, the number of samples with data for the variable is in the "N" column.

Left 4 columns are from the full dataset, right 4 columns are from the subset of subjects with available metabolite data.

Characteristic	N	**Overall**, N = 502,411	**Female**, N = 273,325	**Male**, N = 229,086	N	**Overall**, N = 121,716	**Female**, N = 65,774	**Male**, N = 55,942
Baseline age (21003)	502,411	58 (50, 63)	57 (50, 63)	58 (50, 64)	121,716	58 (50, 63)	57 (50, 63)	58 (50, 64)
Height (cm) (50)	499,870	168 (162, 175)	162 (158, 167)	176 (171, 180)	121,405	168 (162, 175)	162 (158, 167)	176 (171, 180)
BMI (21001)	499,304	26.7 (24.1, 29.9)	26.1 (23.5, 29.7)	27.3 (25.0, 30.1)	121,273	26.7 (24.1, 29.9)	26.1 (23.4, 29.7)	27.3 (25.0, 30.1)
Waist circumference (cm) (48)	500,248	90 (80, 99)	83 (75, 92)	96 (89, 103)	121,482	90 (80, 99)	83 (75, 92)	96 (89, 103)
Hip circumference (cm) (49)	500,189	102 (97, 108)	102 (96, 109)	103 (98, 107)	121,474	102 (97, 108)	102 (96, 108)	103 (98, 107)
Bodyfat % (23099)	492,003	31 (25, 38)	37 (32, 41)	25 (22, 29)	119,515	31 (25, 38)	37 (32, 41)	25 (22, 29)
Trunk fat % (23127)	491,981	31 (26, 37)	35 (29, 40)	28 (24, 32)	119,510	31 (26, 37)	35 (29, 40)	28 (24, 32)
Whole body impedance (23106)	492,224	595 (533, 663)	652 (605, 701)	534 (497, 573)	119,576	595 (533, 663)	652 (605, 701)	535 (497, 574)
Current Smoker (1239)	501,518				121,596			
Prefer not to answer		428 (<0.1%)	220 (<0.1%)	208 (<0.1%)		87 (<0.1%)	48 (<0.1%)	39 (<0.1%)
no		448,128 (89%)	248,293 (91%)	199,835 (87%)		108,814 (89%)	59,826 (91%)	48,988 (88%)
yes		39,231 (7.8%)	18,681 (6.8%)	20,550 (9.0%)		9,488 (7.8%)	4,493 (6.8%)	4,995 (8.9%)
occasionally		13,731 (2.7%)	5,680 (2.1%)	8,051 (3.5%)		3,207 (2.6%)	1,344 (2.0%)	1,863 (3.3%)
Had menopause	272,849				65,709			
Prefer not to answer		534 (0.2%)	534 (0.2%)	0 (NA%)		133 (0.2%)	133 (0.2%)	0 (NA%)
no		64,043 (23%)	64,043 (23%)	0 (NA%)		15,429 (23%)	15,429 (23%)	0 (NA%)
yes		165,380 (61%)	165,380 (61%)	0 (NA%)		39,808 (61%)	39,808 (61%)	0 (NA%)
Not Sure (Hysterectomy)		31,165 (11%)	31,165 (11%)	0 (NA%)		7,574 (12%)	7,574 (12%)	0 (NA%)
Not Sure (Other)		11,727 (4.3%)	11,727 (4.3%)	0 (NA%)		2,765 (4.2%)	2,765 (4.2%)	0 (NA%)
Hysterectomy (ever) (3591)	241,682				58,135			
Prefer not to answer		272 (0.1%)	272 (0.1%)	0 (NA%)		68 (0.1%)	68 (0.1%)	0 (NA%)
Not Sure		257 (0.1%)	257 (0.1%)	0 (NA%)		62 (0.1%)	62 (0.1%)	0 (NA%)
no		221,237 (92%)	221,237 (92%)	0 (NA%)		53,294 (92%)	53,294 (92%)	0 (NA%)
yes		19,916 (8.2%)	19,916 (8.2%)	0 (NA%)		4,711 (8.1%)	4,711 (8.1%)	0 (NA%)
Age at Hysterectomy (2824)	51,031	43 (38, 49)	43 (38, 49)	NA (NA, NA)	12,265	43 (38, 49)	43 (38, 49)	NA (NA, NA)
HRT Use (ever) (2814)	272,846				65,709			
Not Sure		799 (0.3%)	799 (0.3%)	0 (NA%)		191 (0.3%)	191 (0.3%)	0 (NA%)
Prefer not to answer		297 (0.1%)	297 (0.1%)	0 (NA%)		77 (0.1%)	77 (0.1%)	0 (NA%)

Characteristic	N	**Overall**, N = 502,411	**Female**, N = 273,325	**Male**, N = 229,086	N	**Overall**, N = 121,716	**Female**, N = 65,774	**Male**, N = 55,942
no		167,845 (62%)	167,845 (62%)	0 (NA%)		40,394 (61%)	40,394 (61%)	0 (NA%)
yes		103,905 (38%)	103,905 (38%)	0 (NA%)		25,047 (38%)	25,047 (38%)	0 (NA%)
Age started HRT (3536)	103,905	48 (42, 50)	48 (42, 50)	NA (NA, NA)	25,047	48 (42, 50)	48 (42, 50)	NA (NA, NA)
Age last used HRT (3546)	103,905	52 (-1, 57)	52 (-1, 57)	NA (NA, NA)	25,047	52 (-1, 57)	52 (-1, 57)	NA (NA, NA)
Pulse (automated) (102)	467,984	68 (62, 76)	69 (63, 77)	67 (60, 76)	114,537	68 (62, 76)	69 (63, 77)	67 (60, 76)
Systolic BP (manual) (93)	33,102	139 (126, 153)	136 (123, 150)	142 (130, 155)	7,047	139 (126, 153)	136 (123, 150)	142 (130, 155)
Diastolic BP (manual) (94)	33,102	82 (75, 90)	81 (74, 88)	84 (77, 91)	7,047	82 (75, 90)	81 (74, 88)	84 (77, 91)
Diastolic BP (auto) (4079)	467,984	82 (75, 89)	80 (73, 88)	84 (77, 91)	114,537	82 (75, 89)	80 (73, 87)	84 (77, 91)
Systolic BP (auto) (4080)	467,971	138 (126, 152)	135 (122, 150)	141 (130, 154)	114,536	138 (126, 152)	135 (122, 150)	141 (130, 154)
Pulse during BP (manual) (95)	33,102	70 (63, 78)	71 (64, 78)	69 (61, 78)	7,047	70 (63, 78)	70 (64, 78)	68 (62, 77)
Pulse wave arterial stiffness (21021)	169,759	8.99 (6.87, 11.16)	8.27 (6.31, 10.47)	9.78 (7.74, 11.83)	39,314	9.05 (6.92, 11.22)	8.37 (6.35, 10.54)	9.79 (7.75, 11.85)
PEF (3064)	453,610	379 (304, 474)	332 (275, 384)	476 (391, 555)	110,890	380 (305, 477)	333 (276, 385)	478 (392, 556)
HbA1c (30750)	466,414	35.2 (32.8, 37.9)	35.2 (32.7, 37.7)	35.3 (32.8, 38.1)	116,006	35.2 (32.8, 37.9)	35.2 (32.7, 37.7)	35.3 (32.8, 38.1)
Heel BMD (auto, Tscore) (4125)	164,169	-0.39 (-1.09, 0.40)	-0.61 (-1.27, 0.13)	-0.12 (-0.83, 0.69)	38,055	-0.39 (-1.08, 0.40)	-0.61 (-1.26, 0.14)	-0.12 (-0.82, 0.70)
Heel BMD (manual, Tscore) (4138)	1,228	0.60 (0.20, 1.20)	0.60 (0.10, 1.30)	0.60 (0.20, 1.20)	235	0.60 (0.20, 1.20)	0.55 (0.10, 1.23)	0.70 (0.35, 1.20)
Heel bone ultrasound (manual, Tscore) (77)	42,723	-0.30 (-1.10, 0.50)	-0.50 (-1.20, 0.30)	-0.10 (-0.90, 0.70)	11,279	-0.30 (-1.10, 0.50)	-0.50 (-1.20, 0.30)	-0.10 (-0.90, 0.70)
Heel BMD (automated, Tscore) (78)	279,042	-0.46 (-1.15, 0.32)	-0.65 (-1.31, 0.07)	-0.22 (-0.91, 0.58)	69,795	-0.45 (-1.14, 0.33)	-0.65 (-1.31, 0.08)	-0.20 (-0.90, 0.59)
Ethnic Background (21000)	501,511				121,596			
Do not know		217 (<0.1%)	107 (<0.1%)	110 (<0.1%)		49 (<0.1%)	21 (<0.1%)	28 (<0.1%)
Prefer not answer		1,661 (0.3%)	706 (0.3%)	955 (0.4%)		384 (0.3%)	176 (0.3%)	208 (0.4%)
White		569 (0.1%)	244 (<0.1%)	325 (0.1%)		124 (0.1%)	55 (<0.1%)	69 (0.1%)

Characteristic	N	**Overall**, N = 502,411	**Female**, N = 273,325	**Male**, N = 229,086	N	**Overall**, N = 121,716	**Female**, N = 65,774	**Male**, N = 55,942
British		442,516 (88%)	240,213 (88%)	202,303 (88%)		107,700 (89%)	58,084 (88%)	49,616 (89%)
Irish		13,201 (2.6%)	6,894 (2.5%)	6,307 (2.8%)		3,178 (2.6%)	1,641 (2.5%)	1,537 (2.8%)
Other White Background		16,326 (3.3%)	10,037 (3.7%)	6,289 (2.8%)		3,905 (3.2%)	2,359 (3.6%)	1,546 (2.8%)
Mixed		49 (<0.1%)	30 (<0.1%)	19 (<0.1%)		8 (<0.1%)	5 (<0.1%)	3 (<0.1%)
Caribbean		619 (0.1%)	389 (0.1%)	230 (0.1%)		132 (0.1%)	81 (0.1%)	51 (<0.1%)
African		3,818 (0.8%)	1,981 (0.7%)	1,837 (0.8%)		877 (0.7%)	441 (0.7%)	436 (0.8%)
White and Asian		830 (0.2%)	482 (0.2%)	348 (0.2%)		202 (0.2%)	109 (0.2%)	93 (0.2%)
Any other mixed background		1,031 (0.2%)	653 (0.2%)	378 (0.2%)		233 (0.2%)	155 (0.2%)	78 (0.1%)
Asian or Asian British		43 (<0.1%)	23 (<0.1%)	20 (<0.1%)		11 (<0.1%)	6 (<0.1%)	5 (<0.1%)
3001		5,951 (1.2%)	2,939 (1.1%)	3,012 (1.3%)		1,382 (1.1%)	666 (1.0%)	716 (1.3%)
Pakistani		1,835 (0.4%)	715 (0.3%)	1,120 (0.5%)		448 (0.4%)	183 (0.3%)	265 (0.5%)
Bangladeshi		236 (<0.1%)	74 (<0.1%)	162 (<0.1%)		62 (<0.1%)	17 (<0.1%)	45 (<0.1%)
Any other Asian background		1,814 (0.4%)	834 (0.3%)	980 (0.4%)		444 (0.4%)	199 (0.3%)	245 (0.4%)
Black or Black British		27 (<0.1%)	18 (<0.1%)	9 (<0.1%)		7 (<0.1%)	5 (<0.1%)	2 (<0.1%)
4001		4,515 (0.9%)	2,868 (1.1%)	1,647 (0.7%)		1,017 (0.8%)	666 (1.0%)	351 (0.6%)
Other Black Background		123 (<0.1%)	81 (<0.1%)	42 (<0.1%)		21 (<0.1%)	15 (<0.1%)	6 (<0.1%)
Chinese		1,573 (0.3%)	989 (0.4%)	584 (0.3%)		353 (0.3%)	221 (0.3%)	132 (0.2%)
Other ethnic group		4,557 (0.9%)	2,595 (1.0%)	1,962 (0.9%)		1,059 (0.9%)	606 (0.9%)	453 (0.8%)