

Stroke Genetics Network (SiGN)

GWAS of ischemic stroke and its subtypes

Sara L. Pulit

International Stroke Genetics Consortium
Salt Lake City
April 2014

Case cohorts

Cohort	Location	Samples	Array	Cohort	Location	Samples	Array
GASROS	US	470	5M	WUSTL	US	455	5M
GASROS	US	130	610	BASICMAR	Spain	930	5M
GCNKSS	US	499	5M	BRAINS	London	114	5M
GEOS	US	889	1M	BRAINS	London	277	650Q
ISGS	US	372	610	EDIN	Edinburgh	570	660
ISGS	US	187	5M	GRAZ	Austria	639	5M
MCISS	US	630	5M	KRAKOW	Poland	952	5M
MIAMISR	US	299	5M	LEUVEN	Belgium	481	5M
NHS	US	316	5M	LUND	Sweden	651	5M
NOMAS	US	363	5M	MALMO	Sweden	231	OmniExpress
REGARDS	US	311	5M	MUNICH	Germany	1,150	660
SPS3	US	960	5M	OXVASC	UK	464	660
SWISS	US	205	5M	GOTEBURG	Sweden	800	5M
SWISS	US	66	610	STGEORGE	UK	423	660
WHI	US	458	5M	Total	--	14,292	--

Control cohorts

Cohort	Location	Samples	Array
GEOS	US	927	1M
HABC	US	2,802	1M
HRS	US	12,507	2.5M
OAI	US	4,011	2.5M
KRAKOW	Poland	776	5M
LEUVEN	Belgium	468	5M
ADHD	Spain	435	1M
GRAZ	Austria	829	610
INMA	Spain	1,061	1M
KORA	Germany	820	550
WTCCC	UK	5,186	660
MALMO	Sweden	1,419	OmniExpress
Total	--	31,241	--

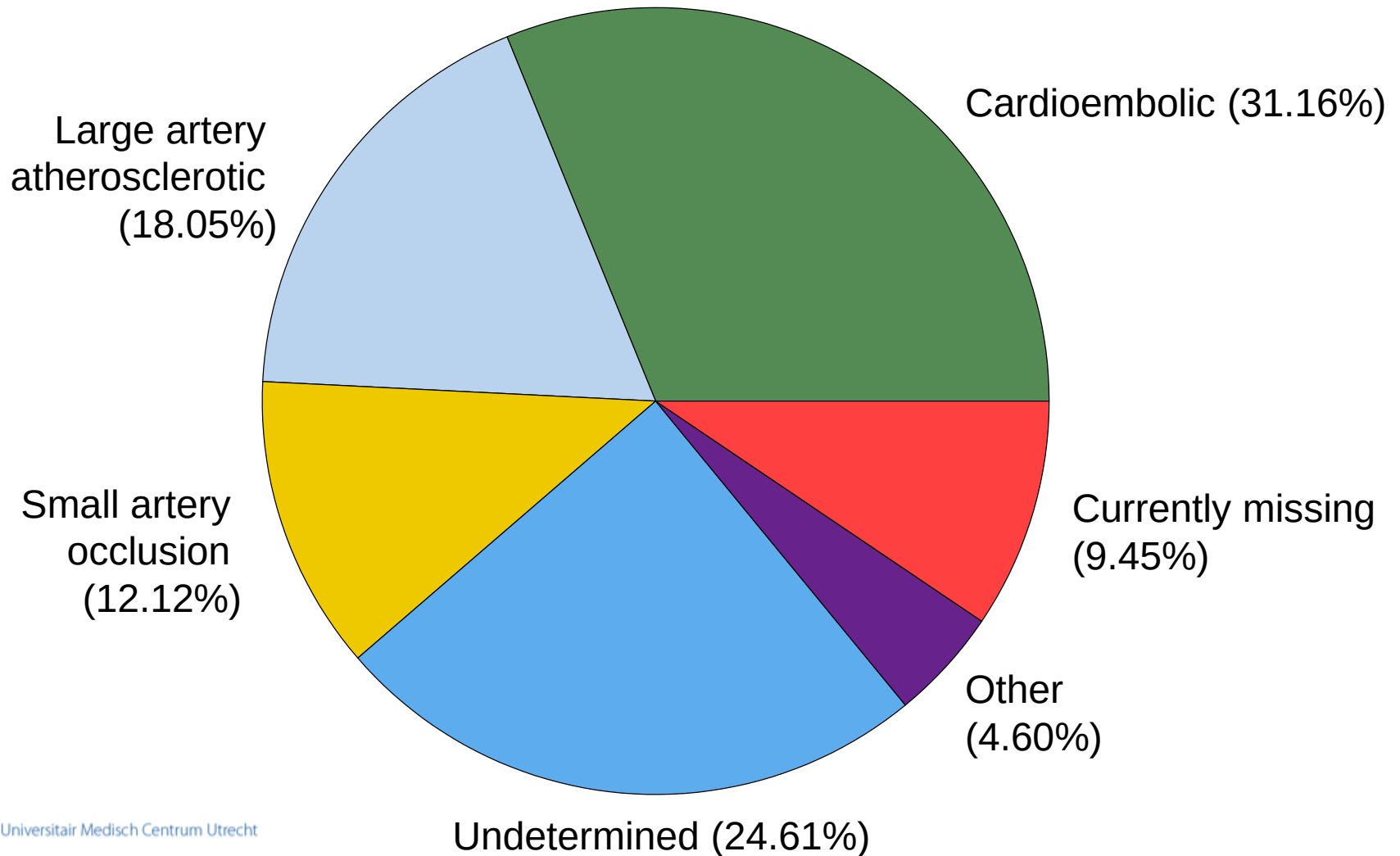
Covariates and risk factors (cases)

	N	% of cases	Missing	% of cases
Total	14,029			
Sex – female	6,523	46.50	0	0
Age	Mean = 61.48 years, SD = 18.49 Median = 65.00 years		313	2.23
Hypertensive	9,221	65.73	351	2.50
Diabetes Mellitus	3,380	24.09	358	2.55
CAD	3,696	26.45	1,035	7.38
Atrial fibrillation	2,940	20.96	653	4.65

After individual cohort QC

Covariates also available in the HRS and OAI control groups

Stroke subtypes (CCS)



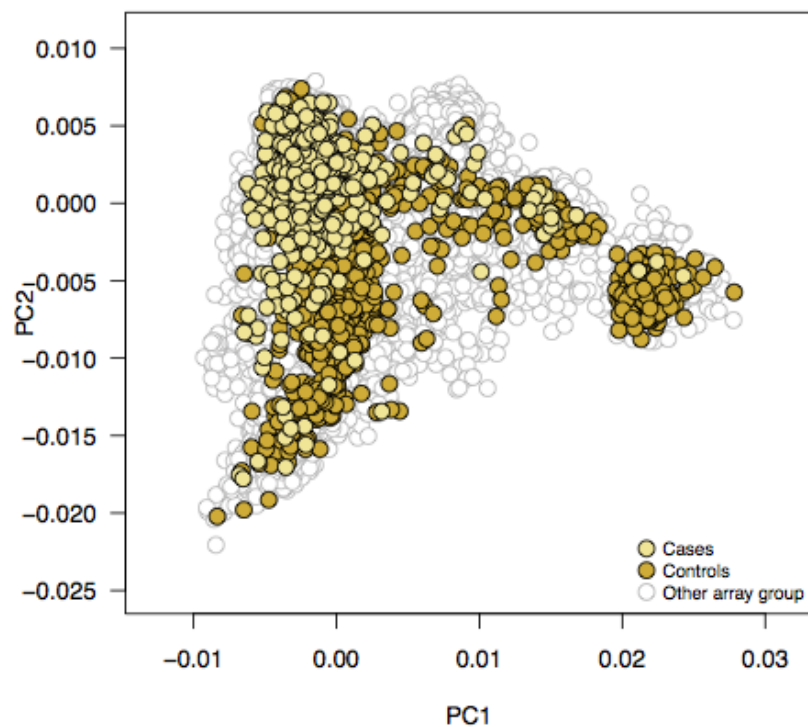
Array groups

Group 1: 610 array	Group 2: 660 array	Group 3: 1M array	Group 4: 2.5M array	Group 5: 5M array
ISGS SWISS GASROS BRAINS GRAZ HABC	EDIN STGEORGE MUNICH OXVASC WTCCC KORA	GEOS ADHD GEOS INMA	CIDR OAI HRS	KRAKOW (cases + controls) LEUVEN (cases + controls)
810 cases 2,476 controls	2,605 cases 5,988 controls	1,774 cases 4,820 controls	9,703 cases 17,748 controls	1,192 cases 1,376 controls
369k SNPs	368k SNPs	773k SNPs	1.87M SNPs	3.3M SNPs

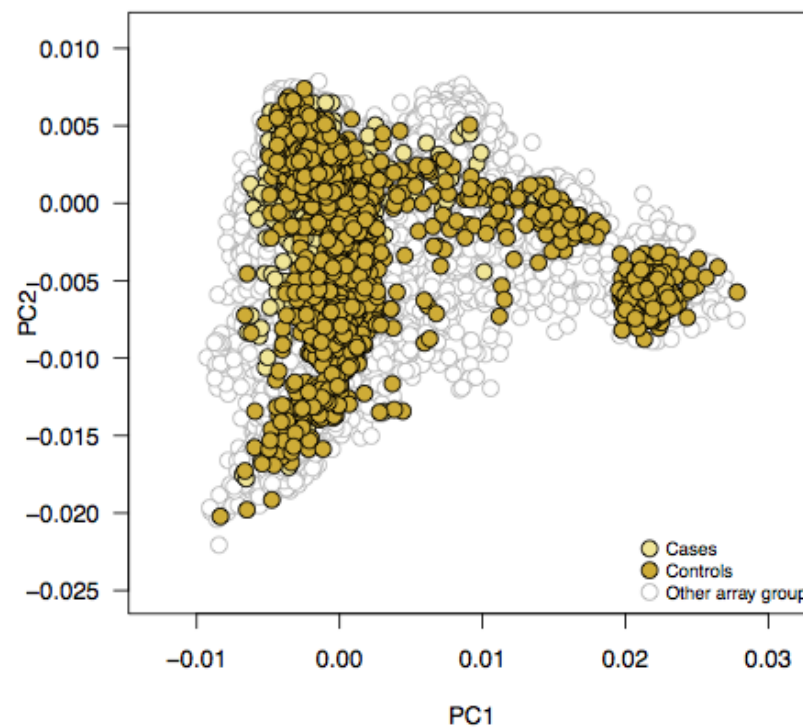
Total N	3277
Cases	810
Controls	2467

Group 1: 610 array

Cases overlaid on controls



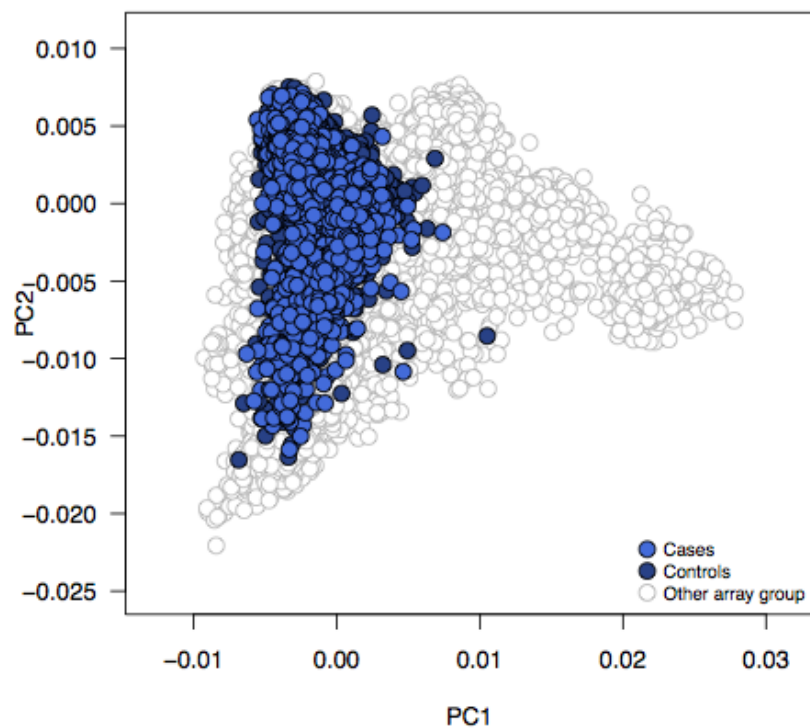
Controls overlaid on cases



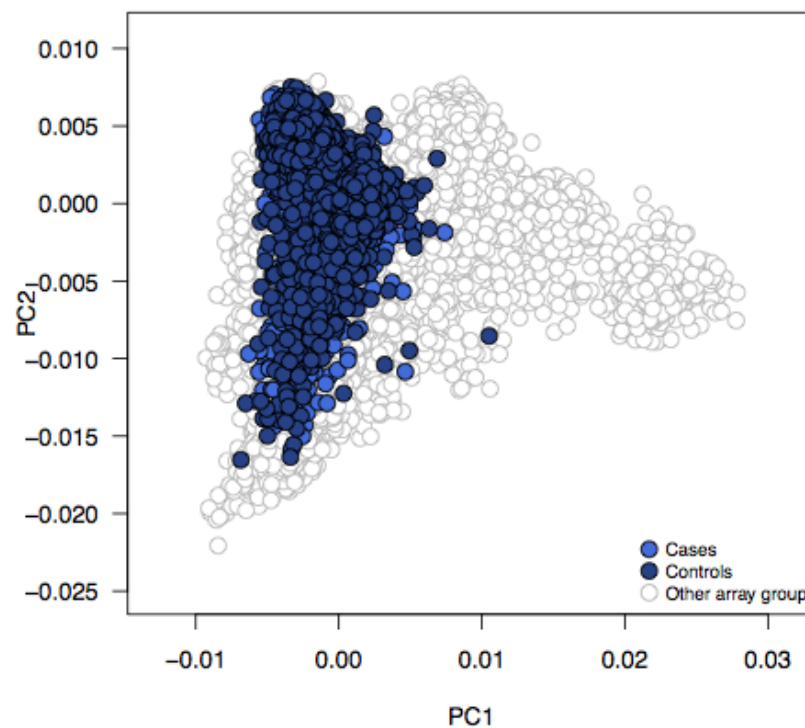
Total N	8541
Cases	2577
Controls	5964

Group 2: 660 array

Cases overlaid on controls



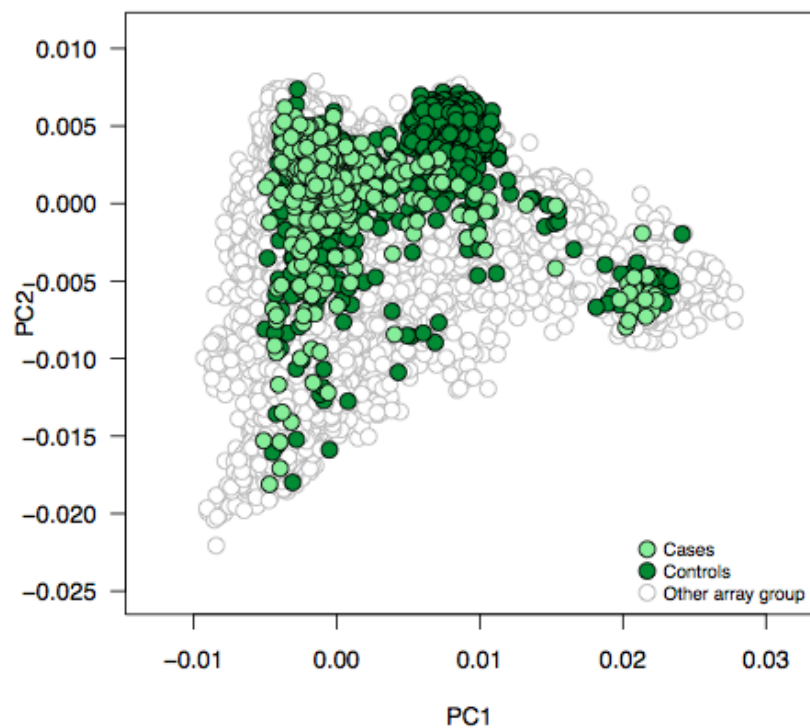
Controls overlaid on cases



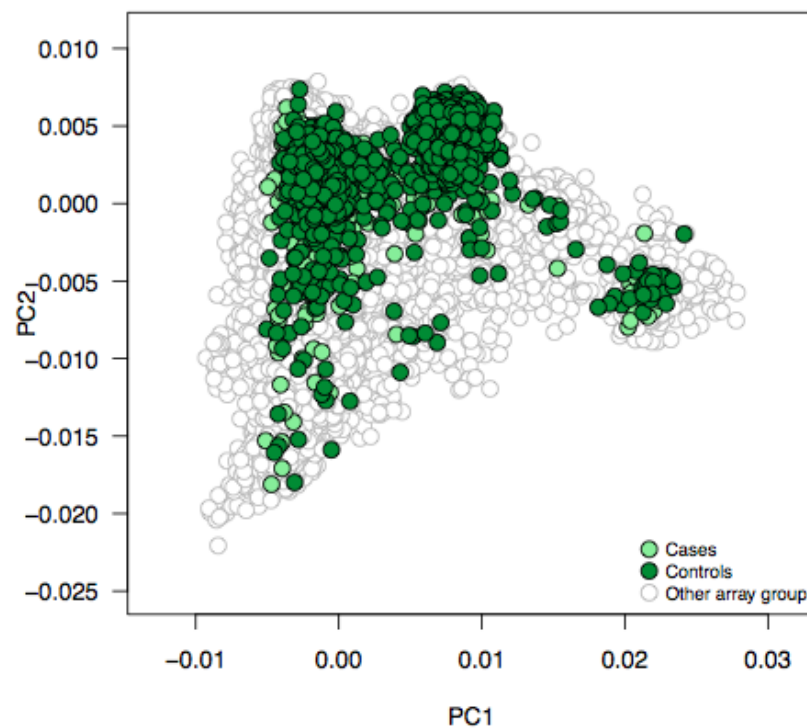
Total N	2475
Cases	464
Controls	2011

Group 3: 1M array

Cases overlaid on controls



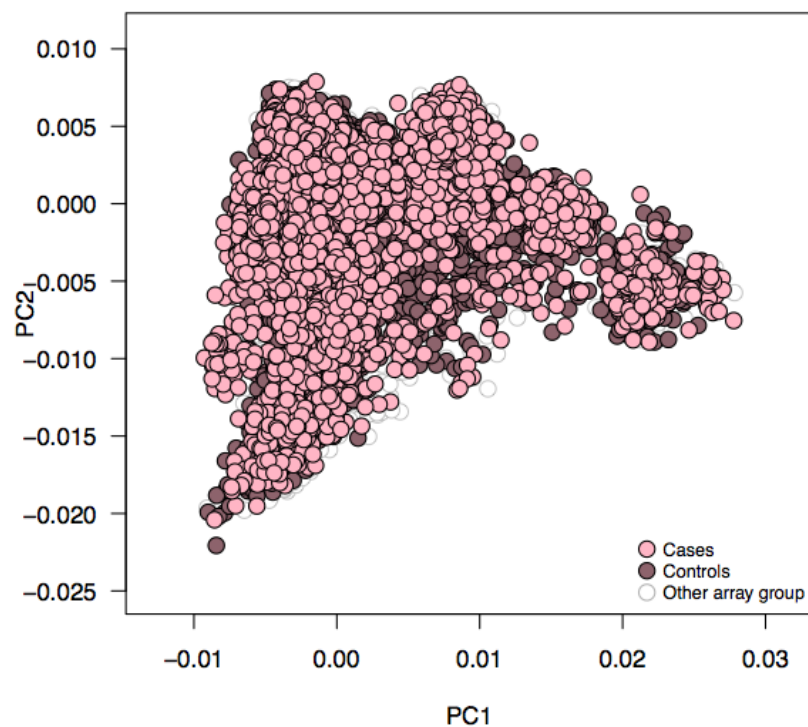
Controls overlaid on cases



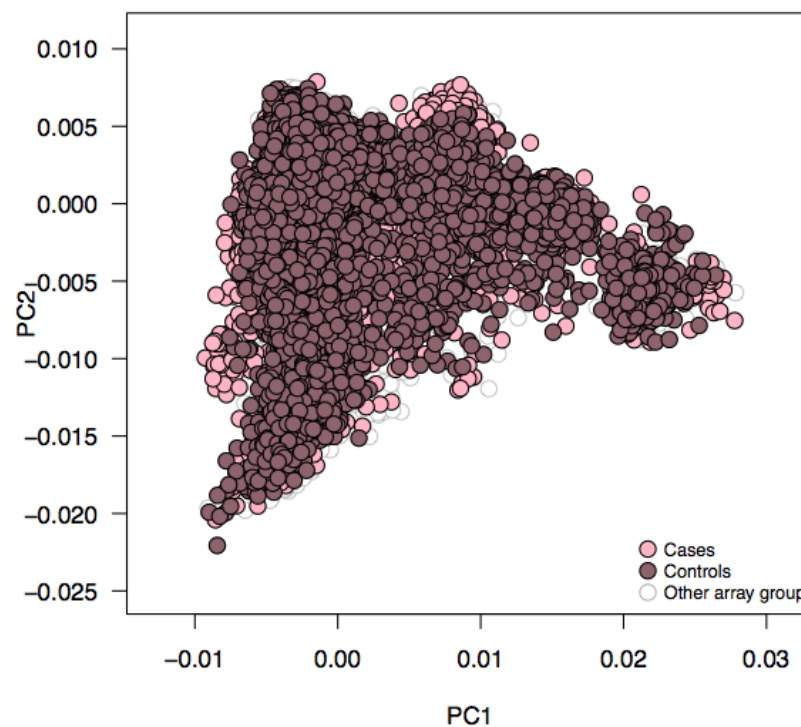
Total N	19104
Cases	6343
Controls	12761

Group 4: 2.5M array

Cases overlaid on controls



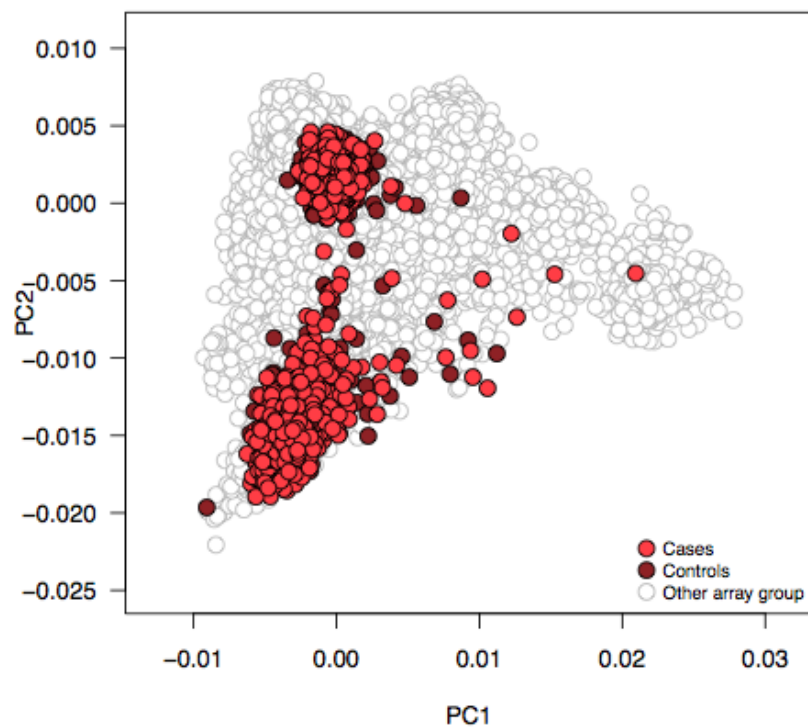
Controls overlaid on cases



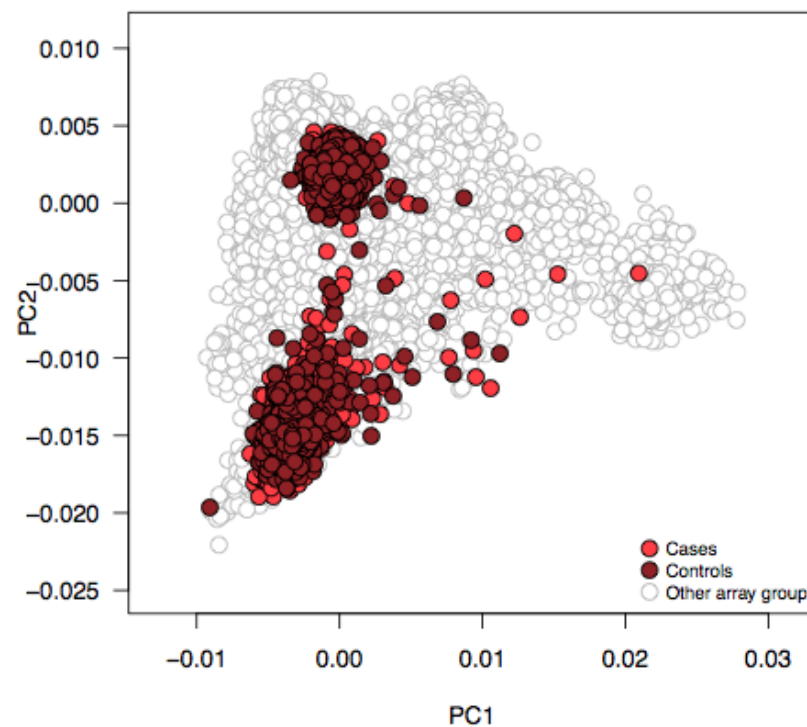
Total N	2519
Cases	1346
Controls	1173

Group 5: 5M array

Cases overlaid on controls



Controls overlaid on cases



Initial case-control strata

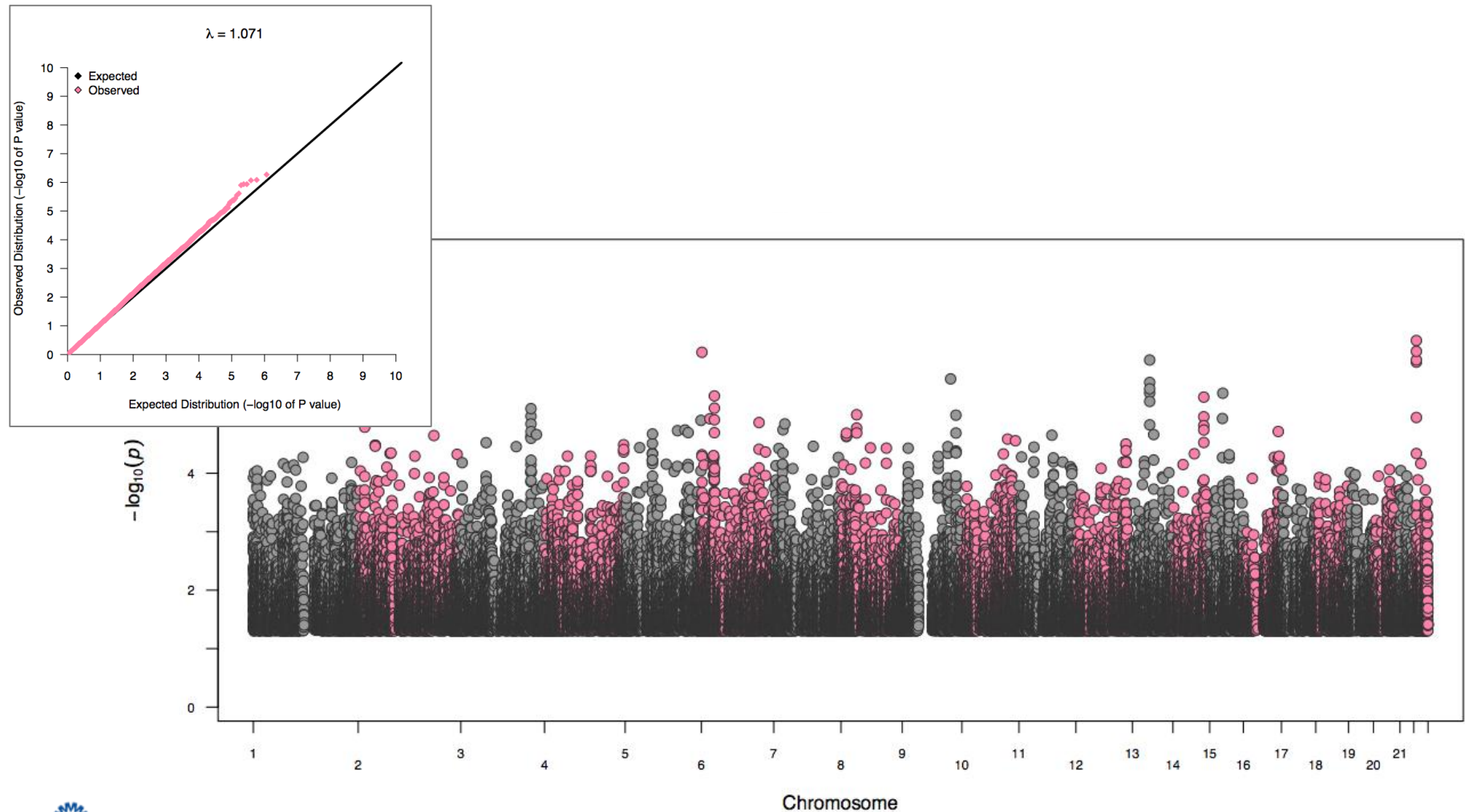
Group	Array	Continent	Cases	Control	Total
1	610	EUR	804	2,438	3,242
2	660	EUR	2,577	5,964	8,541
3	1M	EUR	461	1,992	2,453
4	2.5M	EUR	6,296	12,711	19,007
5	5M	EUR	1,358	1,185	2,543
3	1M	AFR	390	367	757
4	2.5M	AFR	1,229	2,410	3,639
3	1M	ADM	28	30	58
4	2.5M	ADM	571	1,147	1,718

After sample QC

Case-control strata well-behaved

Group	Continent	N	Logistic, no PCs (λ)	Logistic, 10 PCs (λ)
1	EUR	3,242	1.634	1.029
2	EUR	8,541	1.353	1.059
3	EUR	2,453	2.476	1.072
4	EUR	19,007	1.806	0.958
5	EUR	2,543	--	0.814
3	AFR	757	1.020	1.019
4	AFR	3,639	1.479	1.029
3	ADM	58	1.039	1.146
4	ADM	1,718	1.805	0.970

Group 4: 2.5M array – EUR



To do

- Finish definition of strata
 - Waiting for data from Sweden (Malmö)
 - Create separate strata for Spanish (ADHD, INMA and CIDR cases) and Swedish samples
- Imputation
 - Choice of reference panel
- Penultimate association results for Europeans done by end of July
- Admixed groups and chrX need extra time

Acknowledgements

University of Maryland



Brackie Mitchell	Kathy Ryan
Steven Kittner	Huichun Xu
Patrick McArdle	Yuching Cheng
Jeff O'Connell	John Cole
Tushar Dave	Mary J Sparks

UMC Utrecht

Paul de Bakker



University of Virginia

Steve Rich



Univ. of Texas (Houston)

Myriam Fornage



University of Washington



Cathy Laurie
Quenna Wong

LMU Munich

Rainer Malik



Newcastle University

Liz Holliday

