Pakistan Risk of Myocardial Infarction Study (PROMIS) & Risk Assessment of Cerebrovascular Events (RACE)

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The Need

- Mortality attributable to CVD in South Asia expected to double in the next 10 years and become the leading cause of death by 2020

- 80-20 gap

- Immigrant South Asians have higher rates of myocardial infarction and stroke than any other ethnicity in Europe or North America

- Current data are limited: largest available study (INTER-HEART) involved 1700 MI cases and 2200 controls from South Asia

Pakistan Risk Of Myocardial Infarction Study – A bioresource to study the genetic and other determinants of Myocardial Infarction

Pakistan Risk of Myocardial Infarction Study (PROMIS)

- Case – control study of individuals who have suffered a first-ever non-fatal MI frequency matched (by age and sex) to controls free from any cardiovascular diseases

- Planned total collection: 20,000 cases 20,000 controls
  Current recruitment: 5000 cases 5000 controls

Measurements recorded

- 200 item questionnaire tailored to local habits
  (including dietary, lifestyle, socio-economic and family history information)
- Serum (~6ml), plasma (~2ml) and whole blood (~1ml) (stored at -70°C)
- Extracted DNA (stored at -20°C)
- Monocytes, lipid biopsies and other detailed sampling to commence in 2008

Ongoing and planned investigations

- Replication studies as part of Bloodomics and Cardiogenics

- Analyses of variants in ~2000 candidate genes in 4000 participants (in collaboration with the Wellcome Trust Sanger Institute)

- Genome Wide Association Study (GWAS) on 10,000 participants

- Detailed biochemical measurements of lipid fractions, metabolic and other markers

- Genome wide expression (GWE) study (using RNA from monocytes)

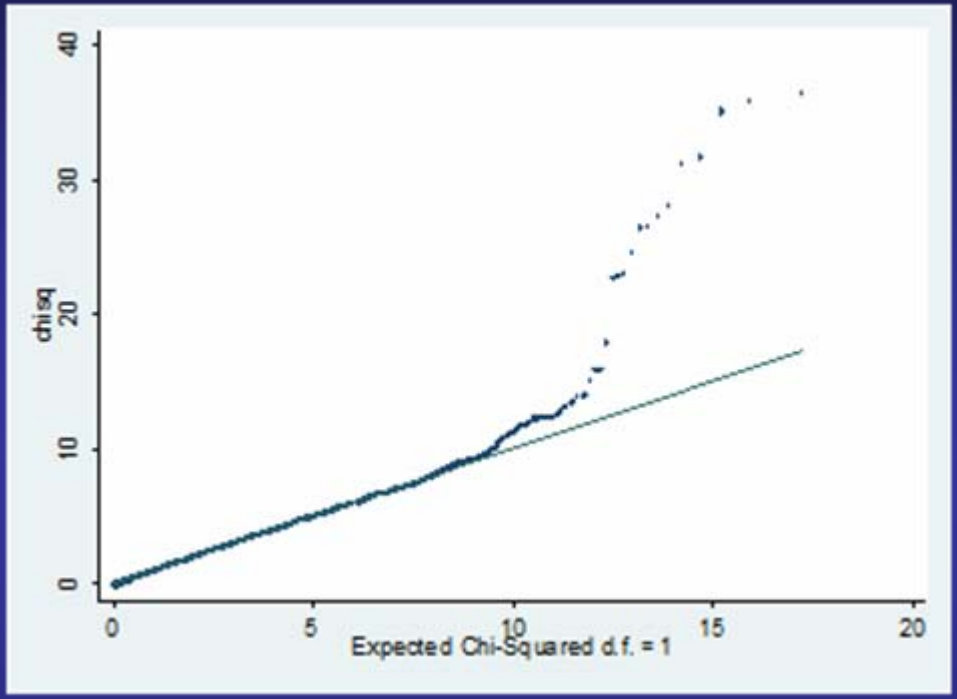
- Metabonomic experiments in serum samples of PROMIS

- Investigation of dietary and lifestyle correlates

Future investigations

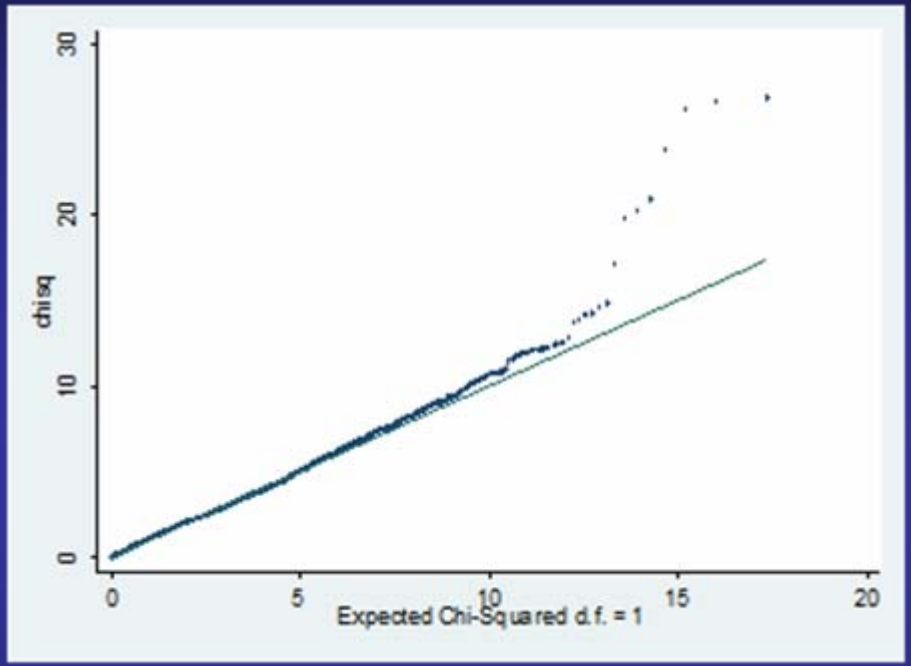
Establishment of cell lines
Investigation of gene-gene and gene-environment interactions

Association with HDL-C levels



Genomic inflation factor: 1

Association with Triglycerides



Genomic inflation factor: 1.

Risk Assessment of Cerebrovascular Events (RACE)

- Risk Assessment of Cerebrovascular Events (RACE) – a bioresource to study the genetic and other determinants of stroke by collecting data from 40,000 participants

- case – control study of individuals who have suffered a first, imaging confirmed stroke frequency matched (by age and sex) to controls free from CVDs

Planned total collection: 20,000 cases 20,000 control
Current recruitment: 1000 cases 1000 controls

Selection of cases

All of the following:

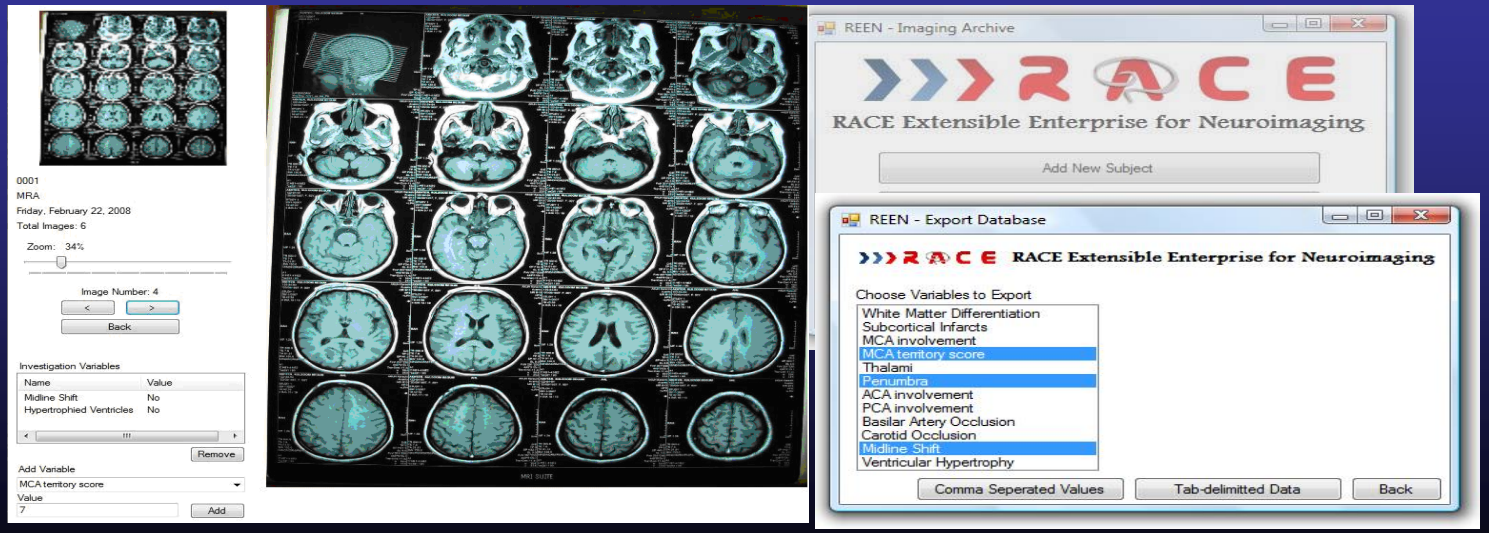
(i) present with a sudden onset of neurological deficit respecting a vascular territory with sustained deficit at 24 hours verified
(ii) older than 15 years;
(iii) the diagnosis is supported by CT/MRI done;
(iv) present with a Modified Rankin Score < 2 prior to the stroke

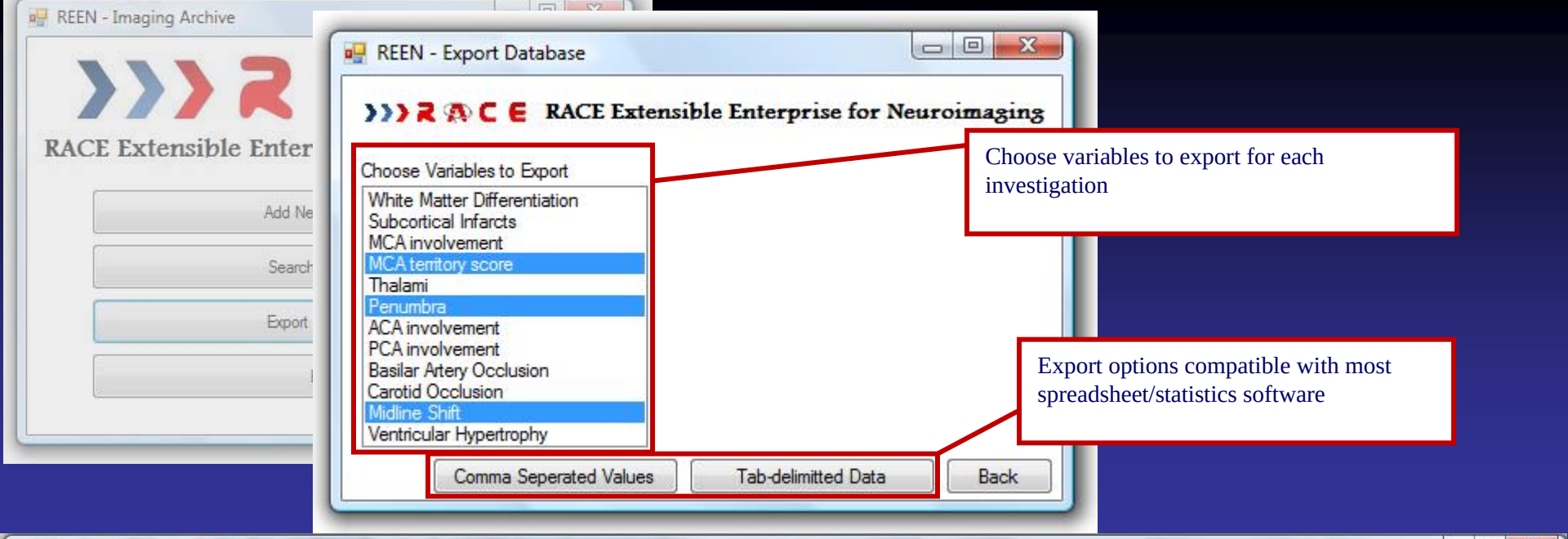


Clinical characterization of cases

• Characterization of cases is done through REEN- a custom made software to maintain a database of all investigations performed on RACE participants

•The TOAST classification method is used to classify ischemic stroke for etiology whereas the Oxfordshire classification is used to classify stroke neuroanatomically.





ReenCSVExport.csv - Microsoft Excel

Home Insert Page Layout Formulas Data Review View

H16

	A	B	C	D	E	F	G	H	I
1	Investigation ID	Subject ID	Subject Center	Investigation Type	Investigation Date	Midline Shift	MCA Territory Score	Basilar Artery Occlusion	Ventricular Hypertrophy
2	1	AKU108	AKU	MRA	2/3/2008	None	10	50%	none
3	2	LNH005	LNH	MRA	4/1/2008	None	10	none	none
4	3	AKU122	AKU	MRA	12/14/2007	None	7	none	none
5	4	JPC214	JPC	CT	3/12/2008	Left	8	25%	none
6	5	KCH012	KCH	CT	1/26/2008	Left	2	90%	none
7	6	AKU004	AKU	MRA	12/22/2007	None	10	80%	none
8	7	AKU003	AKU	MRI	11/29/2007	Right	10	none	none
9	8	LNH007	LNH	MRI	12/4/2007	None	3	none	none
10	9	AKU123	AKU	MRI	4/4/2008	None	8	none	none

Imaging variables available for merger with clinical and biochemical information for further analyses

ReenCSVExport

Ready 100%

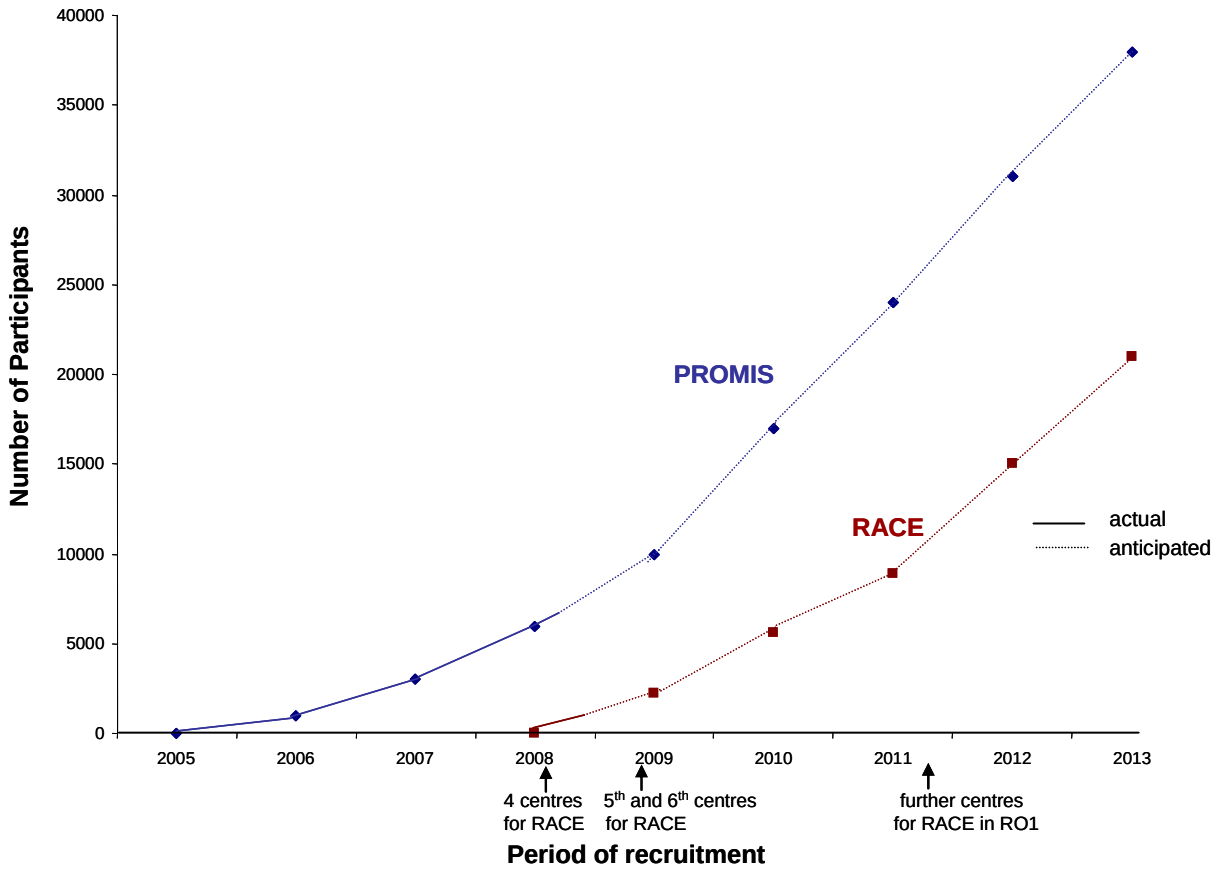
Selection of controls

Prioritized as:

(i) Visitors of patients at the OPD
(ii) Non-blood related visitors of patients without any prior history of CVDs
(iii) Patients visiting the OPD for routine assessment of minor complaints



Rate of recruitment



Measurements recorded

- 200 item questionnaire tailored to local habits
  (including dietary, lifestyle, socio-economic and family history information)

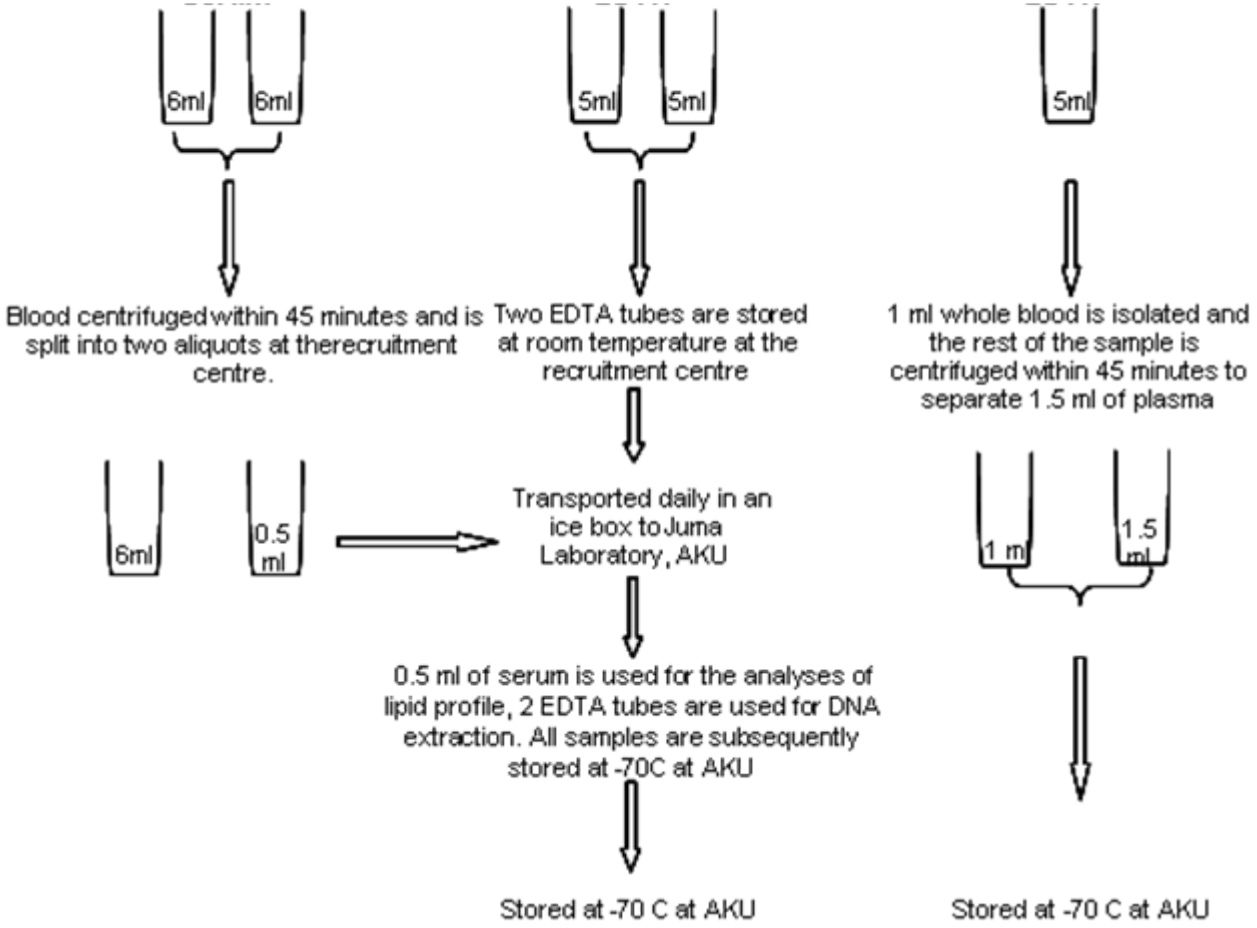
- Serum (~6ml), plasma (~2ml) and whole blood (~1ml) (stored at -70°C)

- Extracted DNA (stored at -20°C)

Questionnaire based information

Type of information	Detail recorded
Symptoms, arrival and management at the hospital	Date of event, time of event, onset of symptoms, time since last meal, review of symptoms, diagnosis and management at the hospital and any investigations ordered by the attending physician.
Medication and medical history	Medication class and duration of use for each of anti-coagulant, blood pressure- and lipid-lowering, diabetes related, hormonal and, for women, contraceptive and HRT medications
Female reproductive history	Age at first menstrual period, age periods stopped, hormones for menopause treatment, number of live born children, age at first delivery, breast-feeding, oral contraceptive
Family history	Approximate age of diagnosis / occurrence of hypertension, diabetes, angina, MI, stroke, cancer or sudden death, for each of mother, father, sister, brother, son and daughter
Ethnicity and other genetic related information	Place of birth, personal and parental ethnicity (eg, Urdu, Punjabi, Pathan, Balooch, Singhi, Memon, Gujrati), personal and paternal co-sanguinity
Socio-economic status	Occupation(s), monthly income, level and duration of education, marital status, no. of dependants, ownership / wealth
Physical activity	Type, frequency, duration and intensity of activity for each of occupational, work related commuting and leisure time
Tobacco consumption	For each type of tobacco (cigarettes, beedies, huqqa, paan, naswar, gutka and supari), usage status, quantity, frequency and lifetime. Information on sources of passive smoking also recorded
Psychosocial factors	Experience of traumatic events in the past year (eg, loss of crop, family bereavement), perceived level of occupational, domestic and financial stress, perceived level of mental and physical health
Anthropometry	Height, weight, waist and hip circumference.
Food frequency questionnaire	A 60-item locally validate FFQ pertaining information on alcohol, ghee and oil consumption, fruits and vegetables, breads, meats, legumes, tea and beverages and sweets

Sample Collection Procedures



Preliminary Results

Field teams based in 11 recruitment centres

1 x study coordinator

11 x recruitment coordinators (1 at each centre)

44 x research medical officers (4 at each centre)

55 x phlebotomists (6 at each centre)

Staff at the national coordinating centre- (AKUH)

6 x laboratory research associates

6 x data entry nosologists

1 x financial manager

Future Directions

- GWAS in RACE and other studies – Added value provided through already genotyped controls in PROMIS
- Mechanistic studies on novel loci detected in South Asians through GWAS and other approaches
- Availability of samples for replication-validation studies in other populations

Thank You