UK Biobank

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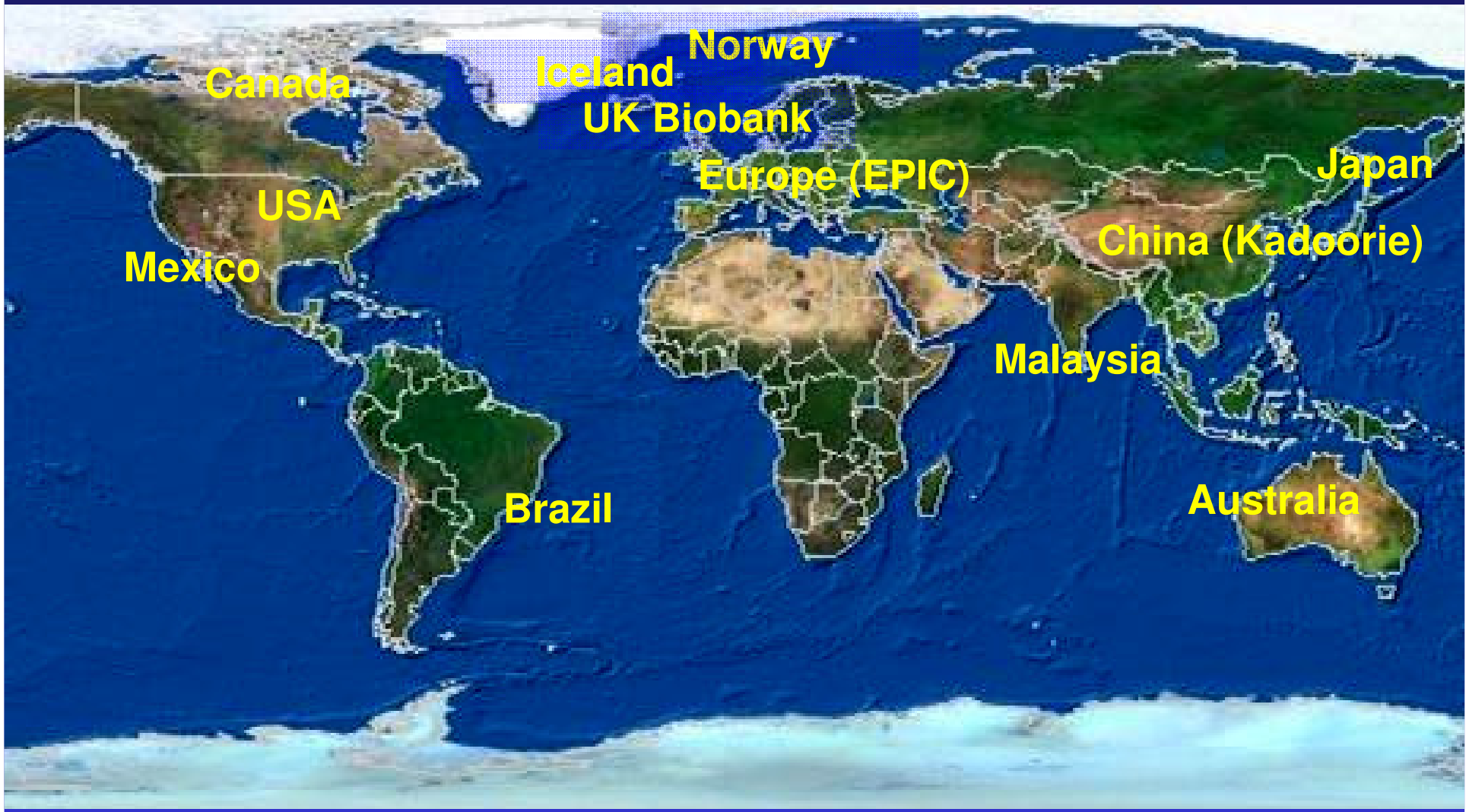
Selected biobank studies (planned or existing)



Two largest blood-based studies

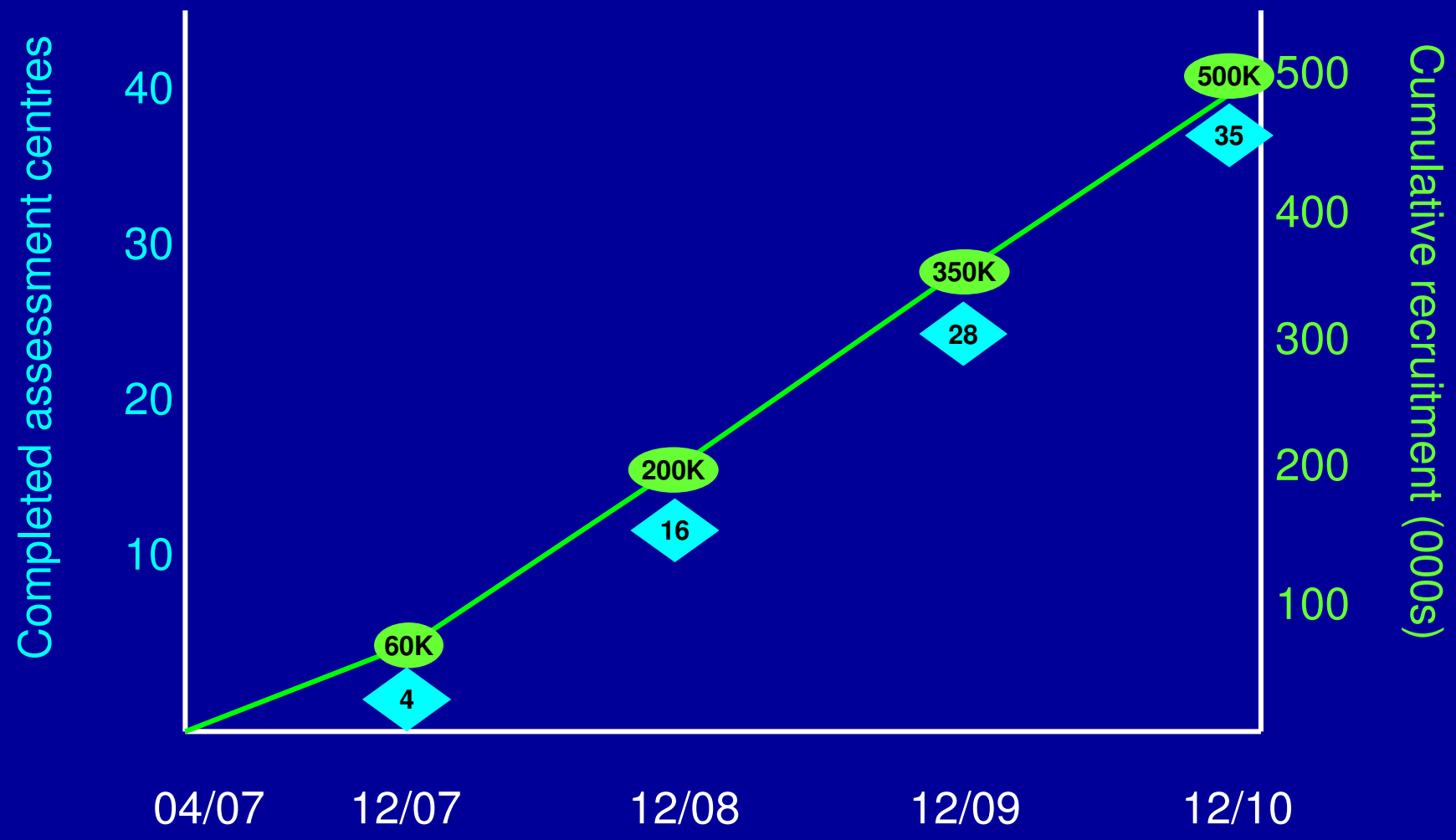
Kadoorie (China), 2004-8 500,000

UK Biobank, 2006-10 500,000

Both ask many questions, make many physical measurements, store blood & periodically resurvey tens of thousands.

Follow up all treated episodes of illness (not just cause-specific mortality)

UK Biobank: Timetable for assessment of 0.5M participants during 2007-10



UK Biobank Prospective Study

- 0.5M UK men and women aged 40-69
- Extensive baseline questions and physical measures, as well as stored blood and urine samples that allow many different types of analysis in the future
- General consent from participants for follow-up through all health-related records & for unspecified health research (with no feedback of individual results)

Identification & invitation of participants: efficient, centrally-administered process

- UK Biobank processes contact details from central registries, in confidence, to generate invitations cost-effectively

- Central invitation and appointment system aids high throughput and smooth running of assessment centres

UK Biobank Prospective Study

- 0.5M UK men and women aged 40-69
- Invite %M to recruit 0.5M; not randomly representative of UK, but still informative
- Recruitment rate varies from <10% to >20% depending on proximity to unit

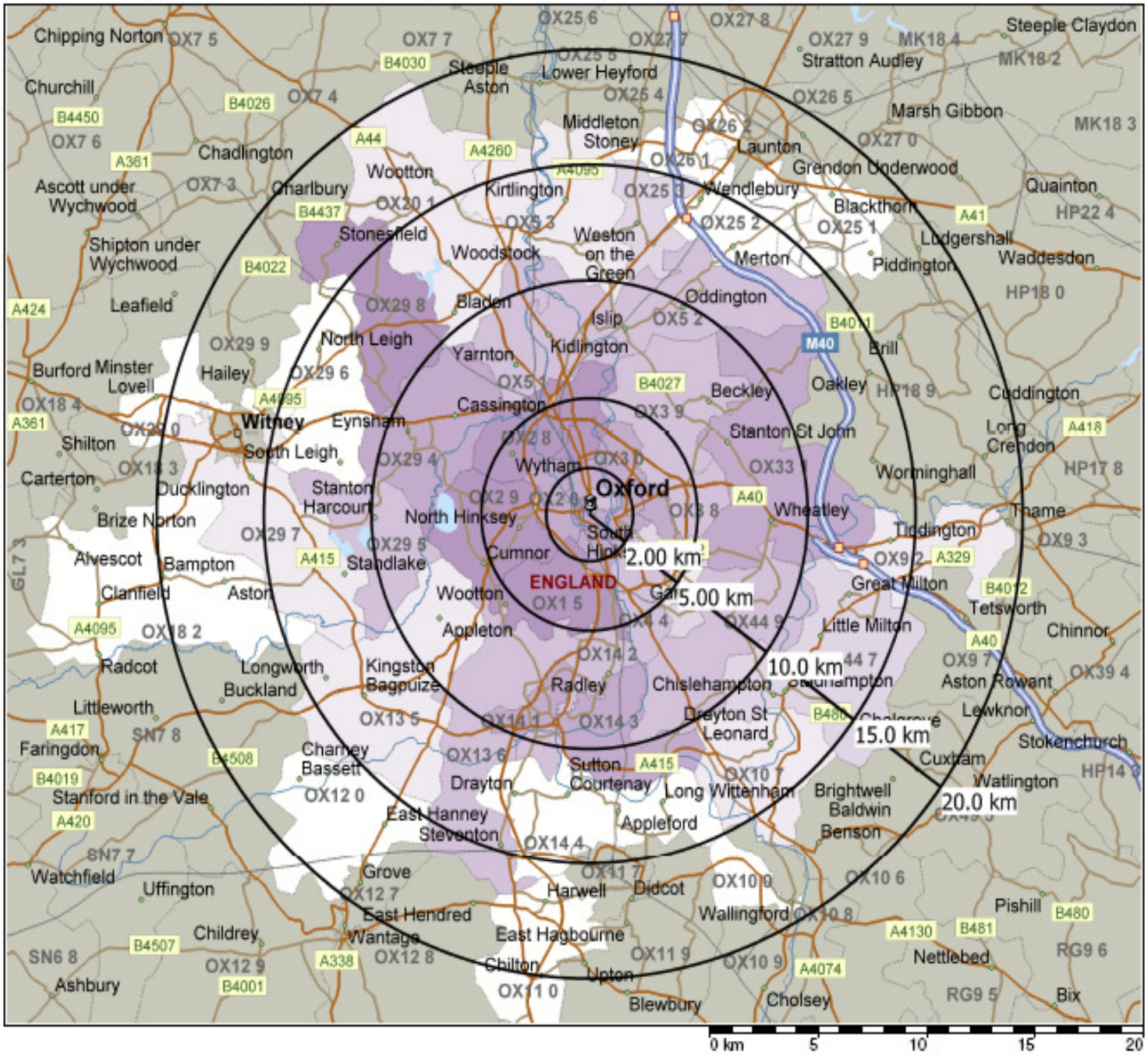
Oxford Confirmation Rate by Postcode Sector 10 July 2007

Confirmed by Postcode Sector divided by Invitations

- 0.175 to 0.200
- 0.150 to 0.174
- 0.125 to 0.149
- 0.100 to 0.124
- 0.075 to 0.099
- 0.050 to 0.074
- 0.025 to 0.049
- 0.000 to 0.024

Pushpins

- 20070702Invitebreakdown
- My Pushpins



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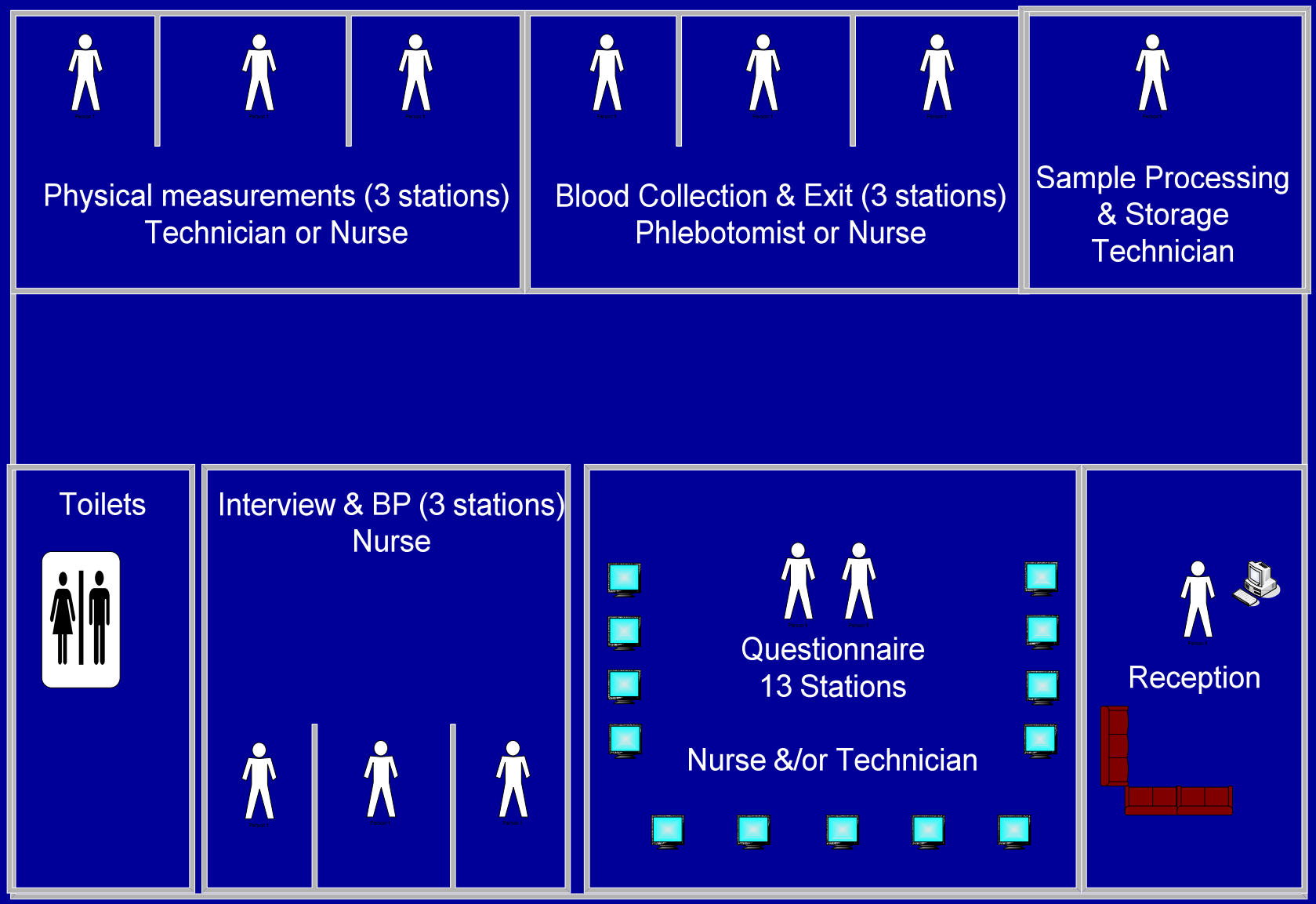
Streamlined assessment centre flow: ~110 people/day in ~6 concurrent centres



Careful design and piloting of streamlined assessment centre visit (~90 minutes total)

- Efficient and low cost touch-screen system used for consent and most questions (inc. cognition/reaction)
- Computer-assisted interview for limited questions (e.g. medications, medical history, occupation)
- Participant moves smoothly through standardised stations (questions; measures; samples)
- Dedicated staff at each station, plus senior managing nurse, ensure high throughput (>100/day/centre)
- Assessment centres conveniently located, and open in early mornings/evenings and at weekends

Biological sample collection and handling

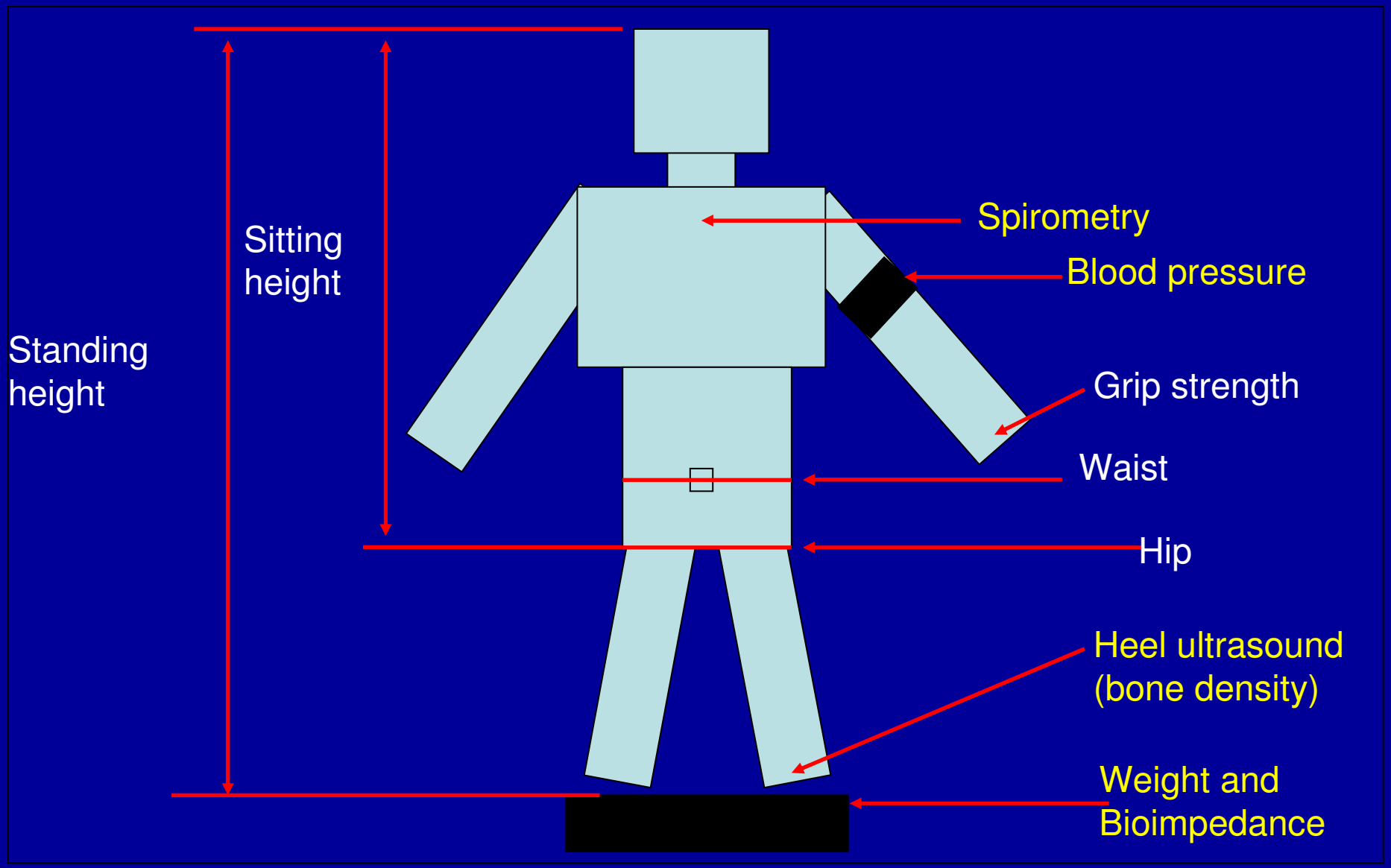
Vacutainer tube	Fractions	Number of aliquots	
		-80ºC	Liquid N_2
EDTA (9ml) x 2	Plasma	6	2
	Buffy coat	2	2
	Red cells	-	2
Lithium Heparin (PST)	Plasma	3	1
Clot activator (SST)	Serum	3	1
ACD	DMSO blood	-	2
EDTA (4 ml)	Haematology (immediate)	-	-
Urine	Urine	4	2
TOTAL ALIQUOTS		18	12

Advantages of “nested” case-control approach to sample assays

- Assays need to be conducted only on relatively small subset (e.g. few thousand or tens of thousands)
  - Substantially reduces costs of assays
  - Minimises depletion of limited sample
  - Facilitates good quality control
- Assays need to be conducted only after sufficient numbers of relevant disease cases have occurred
  - Specific hypotheses will be clearer after delay
  - Wider range of assays possible at lower cost

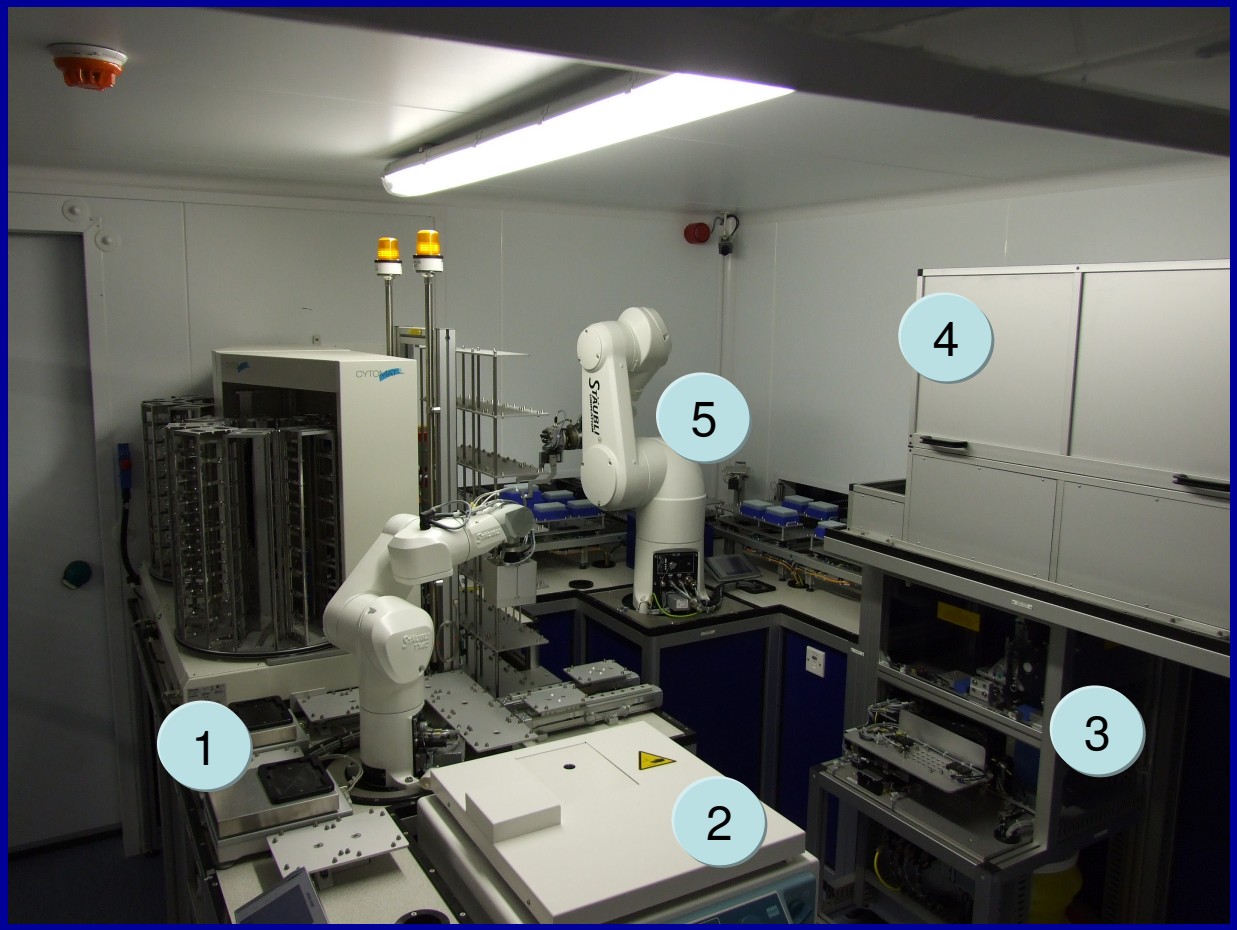
UK Biobank: physical measures included

(data entry: yellow=auto; white=manual)



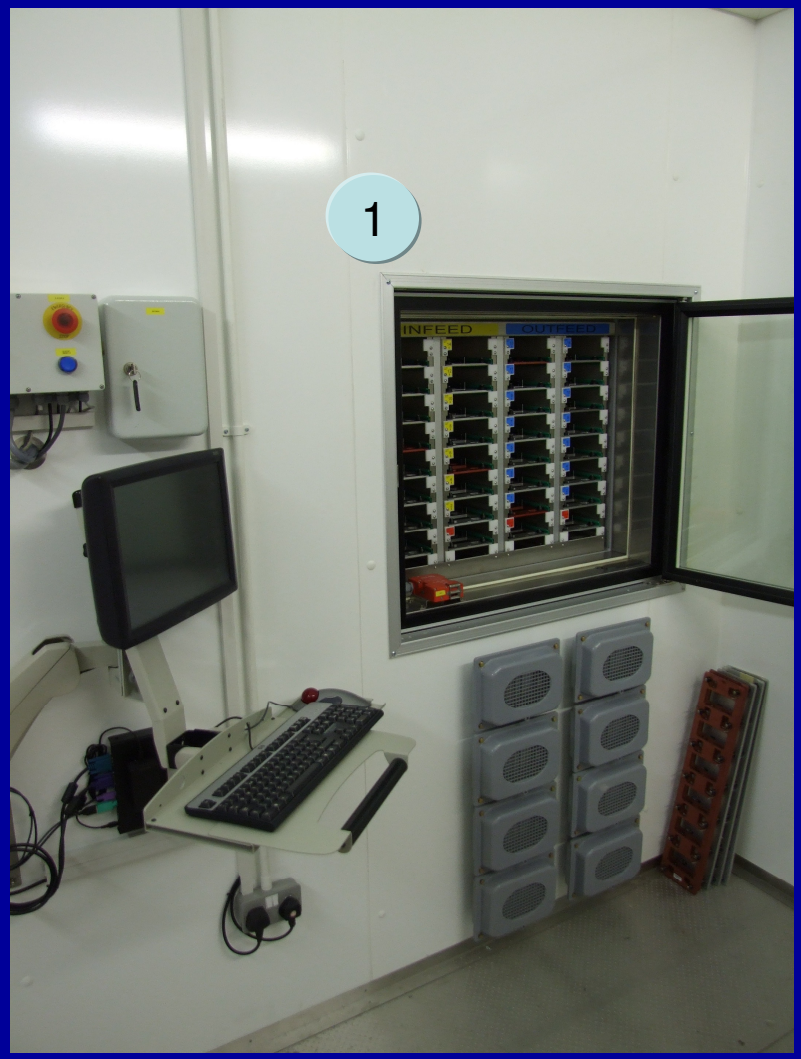
Topic Areas	Median Touch screen time (mins)	Topic Areas	Median Touch screen time (mins)
Socio-demographics	3.0	Ethnicity	0.2
Tobacco smoking	0.5	Family history, sib-linkage, twins	1.9
Physical Activity	4.5	Psychological state	2.4
Diet	4.6	Screen/health service use	0.3
Alcohol consumption	1.0	Sex specific questions	1.7 (f) 0.4 (m)
Sleep	1.2	Past medical history/medications	1.8
Early childhood	1.2	Other general health & disability	3.2
Environmental exposures	3.3	Cognitive Function	4.2

UK Biobank: Automated separation of blood



1. Automated balancing
2. Centrifugation
3. De-capping
4. Vision system detects fraction boundaries
5. Liquid aliquoting

UK Biobank: -80°C automated sample archive

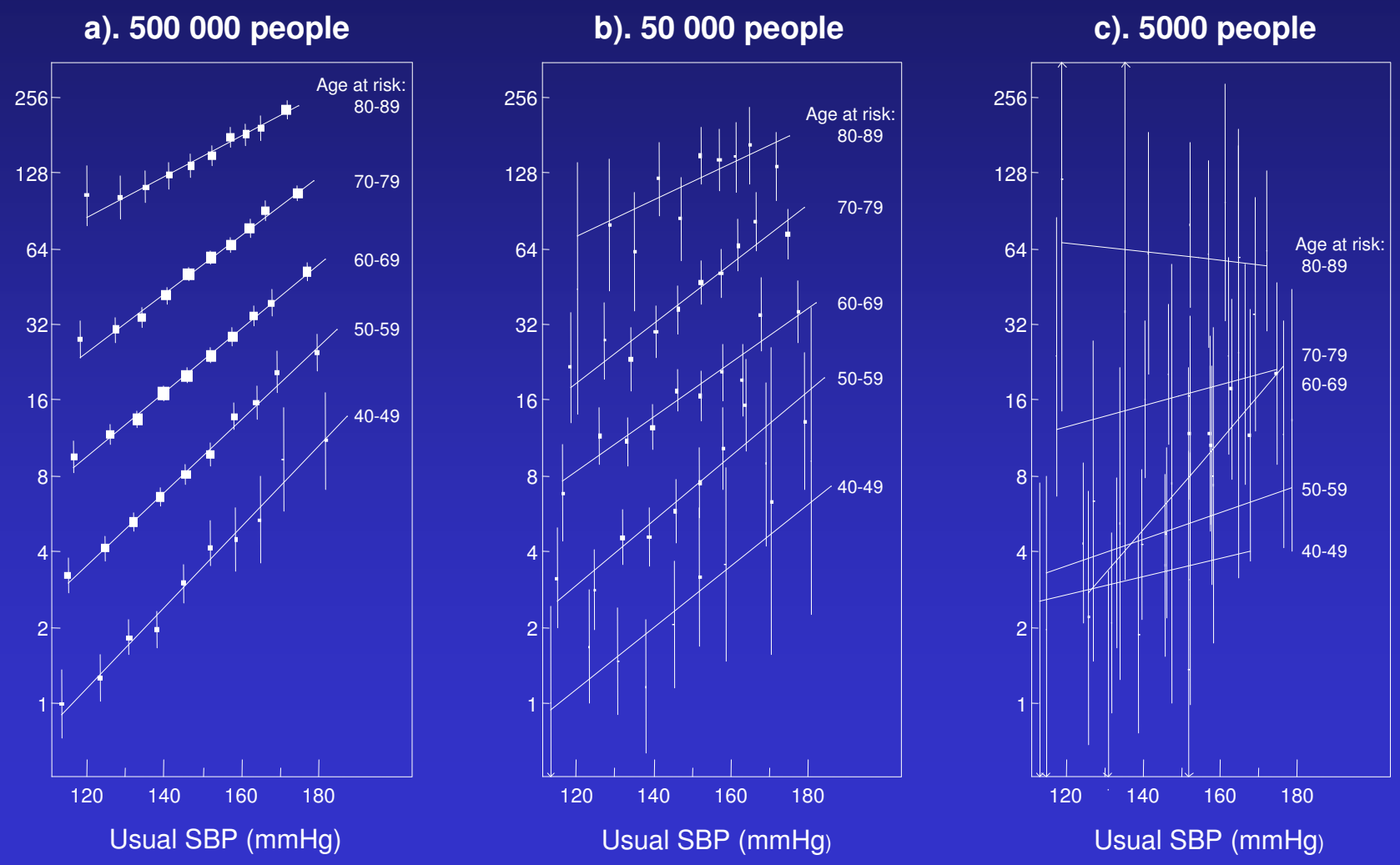


1. Dry-air lock 2. -20°C aisle robotics 3. -80°C storage drawers

Long-term follow-up of health-related exposures and outcomes through different sources

- Consent obtained from participants for access to their past and future medical and other health-related records:
  - *Death & cancer:* already available through UK central registries
  - *Hospitalisations:* already available in Scotland (SMR) and in England & Wales (HES)
  - *Primary care, medications & investigations:* already available in Scotland

Size matters: Informativeness of 0.5M *vs* 50K *vs* 5K people on relation of SBP and IHD in PSC



Prospective Studies Collaboration investigators

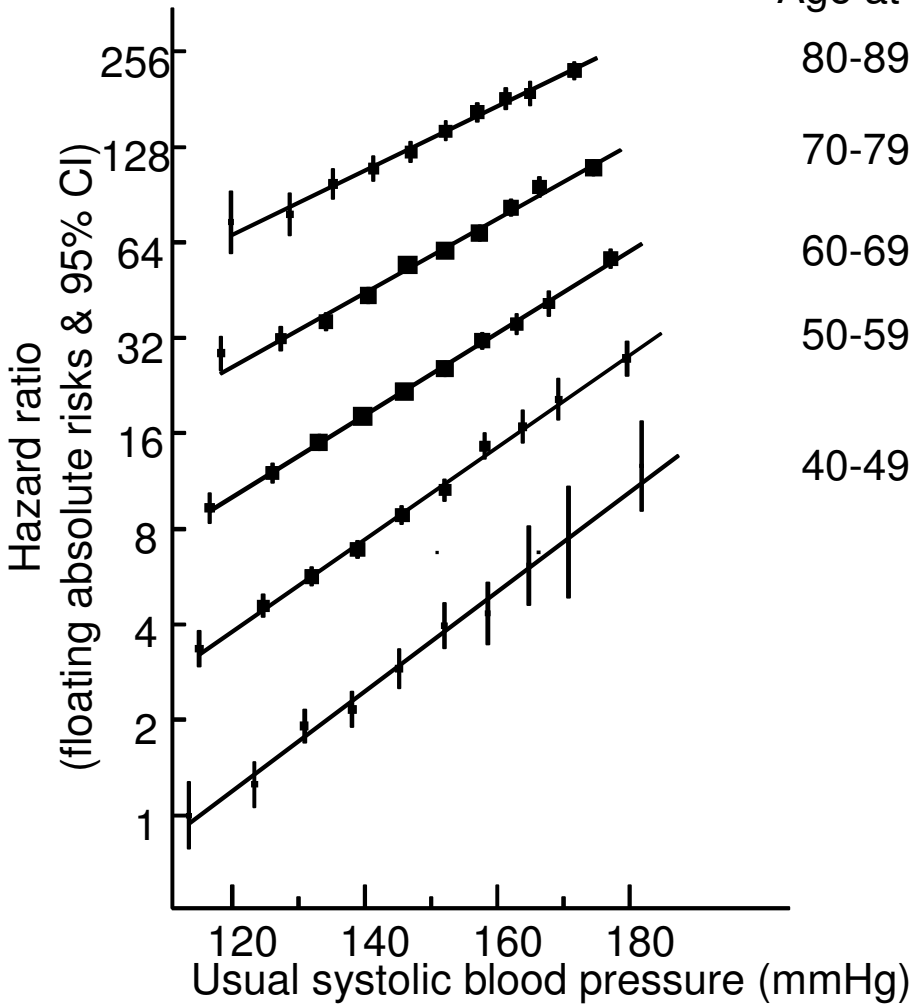
Atherosclerosis Risk in Communities (ARIC): L Chambless; *Belgian Inter-university Research on Nutrition and Health (BIRNH):* G De Backer, D De Bacquer, M Kornitzer; *British Regional Heart Study (BRHS):* P Whincup, SG Wannamethee, R Morris; *British United Provident Association (BUPA):* N Wald, J Morris, M Law; *Busselton:* M Knuiman, H Bartholomew; *Caerphilly and Speedwell:* G Davey Smith, P Sweetnam, P Elwood, J Yarnell; *Cardiovascular Health Study (CHS):* R Kronmal; *CB Project:* D Kromhout; *Charleston:* S Sutherland, J Keil; *Copenhagen City Heart Study:* G Jensen, P Schnohr; *Evans County:* C Hames (deceased), A Tyroler; *Finnish Mobile Clinic Survey (FMCS):* A Aromaa, P Knekt, A Reunanen; *Finrisk:* J Tuomilehto, P Jousilahti, E Vartiainen, P Puska; *Flemish Study on Environment, Genes and Health (FLEMENGHO):* T Kuznetsova, T Richart, J Staessen, L Thijs; *Research Centre for Prevention and Health (Glostrup Population Studies):* T Jorgensen,T Thomsen; *Honolulu Heart Program:* D Sharp, JD Curb; *Ikawa, Noichi and Kyowa:* H Iso, S Sato, A Kitamura, Y Naito; *Imperial College, London* and *Oxon Clinical Epidemiology Limited*: N Qizilbash; *Centre d'Investigations Preventives et Cliniques (IPC), Paris:* A Benetos, L Guize; *Israeli Ischaemic Heart Disease Study:* U Goldbourt; *Japan Railways:* M Tomita, Y Nishimoto, T Murayama; *Lipid Research Clinics Follow-up Study (LRC):* M Criqui, C Davis; *Midspan Collaborative Study:* C Hart, G Davey-Smith, D Hole, C Gillis; *Minnesota Heart Health Project (MHHP)* and *Minnesota Heart Survey (MHS):* D Jacobs, H Blackburn, R Luepker; *Multiple Risk Factor Intervention Trial (MRFIT):* J Neaton, L Eberly; *First National Health and Nutrition Examination Survey Epidemiologic Follow-up Study (NHEFS):* C Cox; *NHLBI Framingham Heart Study:* D Levy, R D'Agostino, H Silbershatz; *Norwegian Counties Study:* A Tverdal, R Selmer; *Northwick Park Heart Study (NPHS):* T Meade, K Garrow, J Cooper; *Nurses' Health Study:* F Speizer, M Stampfer; *Occupational Groups (OG), Rome:* A Menotti, A Spagnolo; *Ohasama:* I Tsuji, Y Imai, T Ohkubo, S Hisamichi; *Oslo:* L Haheim, I Holme, I Hjermann, P Leren; *Paris Prospective Study:* P Ducimetiere, J Empana; *Perth:* K Jamrozik, R Broadhurst; *Prospective Cardiovascular Munster Study (PROCAM):* G Assmann, H Schulte; *Prospective Study of Women in Gothenburg:* C Bengtsson, C Björkelund, L Lissner; *Puerto Rico Health Heart Program (PRHHP):* P Sorlie, M Garcia-Palmieri; *Rancho Bernado:* E Barrett-Connor, M Criqui, R Langer; *Renfrew and Paisley study:* C Hart, G Davey Smith, D Hole; *Saitama Cohort Study:* K Nakachi, K Imai; *Seven Cities China:* X Fang, S Li; *Seven Countries (SC) Croatia:* R Buzina; *SC Finland:* A Nissinen; *SC Greece (Greek Islands Study):* C Aravanis, A Dontas, A Kafatos; *SC Italy:* A Menotti; *SC Japan:* H Adachi, H Toshima, T Imaizumi; *SC Netherlands:* D Kromhout; *SC Serbia:* S Nedeljkovic, M Ostojic; *Shanghai:* Z Chen; *Scottish Heart Health Study (SHHS):* H Tunstall-Pedoe; *Shibata:* T Nakayama, N Yoshiike, T Yokoyama, C Date, H Tanaka; *Tecumseh:* J Keller; *Tromso:* K Bonaa, E Arnesen; *United Kingdom Heart Disease Prevention Project (UKHDPP):* H Tunstall-Pedoe; *US Health Professionals Follow-up Study:* E Rimm; *US Physicians' Health Study:* M Gaziano, JE Buring, C Hennekens; *Värmland:* S Törnberg, J Carstensen; *Whitehall:* M Shipley, D Leon, M Marmot; *Clinical Trial Service Unit (CTSU):* J Armitage, C Baigent, Z Chen, R Clarke, R Collins, J Emberson, J Halsey, M Landray, S Lewington, A Palmer (deceased), S Parish, R Peto, P Sherliker, G Whitlock.

Steering Committee — S Lewington (coordinator and statistician), S MacMahon (chair), R Peto (statistician), A Aromaa, C Baigent, J Carstensen, Z Chen, R Clarke, R Collins, S Duffy, D Kromhout, J Neaton, N Qizilbash, A Rodgers, S Tominaga, S Törnberg, H Tunstall-Pedoe, G Whitlock.

PSC http://www.ctsu.ox.ac.uk/projects/psc/

PSC: CHD mortality in each decade of age versus usual SBP at the start of that decade

33 867 deaths at ages 40 - 89

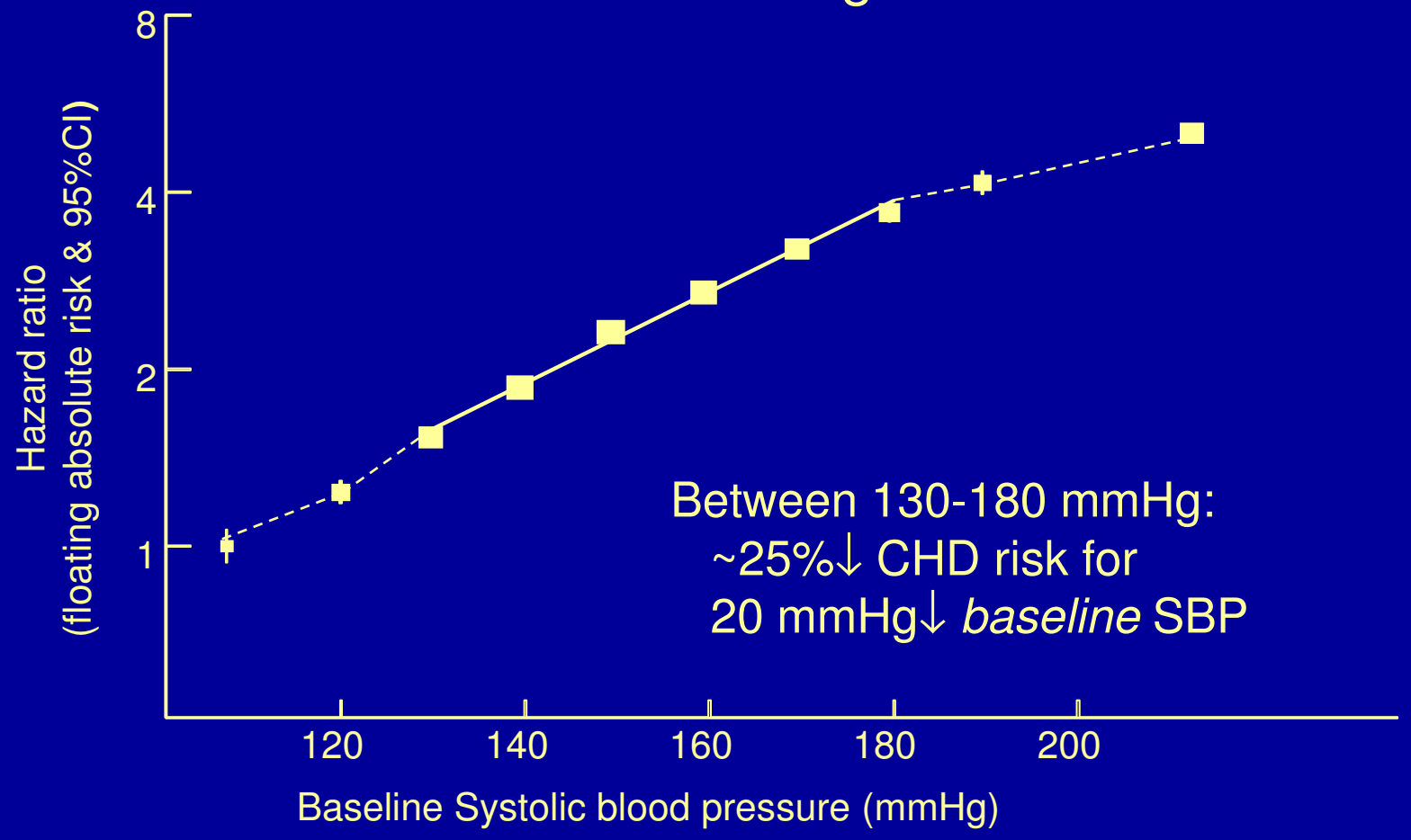


Age at risk	20 mmHg ↓ SBP
80-89	31% ↓ risk
70-79	40% ↓ risk
60-69	46% ↓ risk
50-59	50% ↓ risk
40-49	51% ↓ risk

Lancet 2002; 360:1903-13

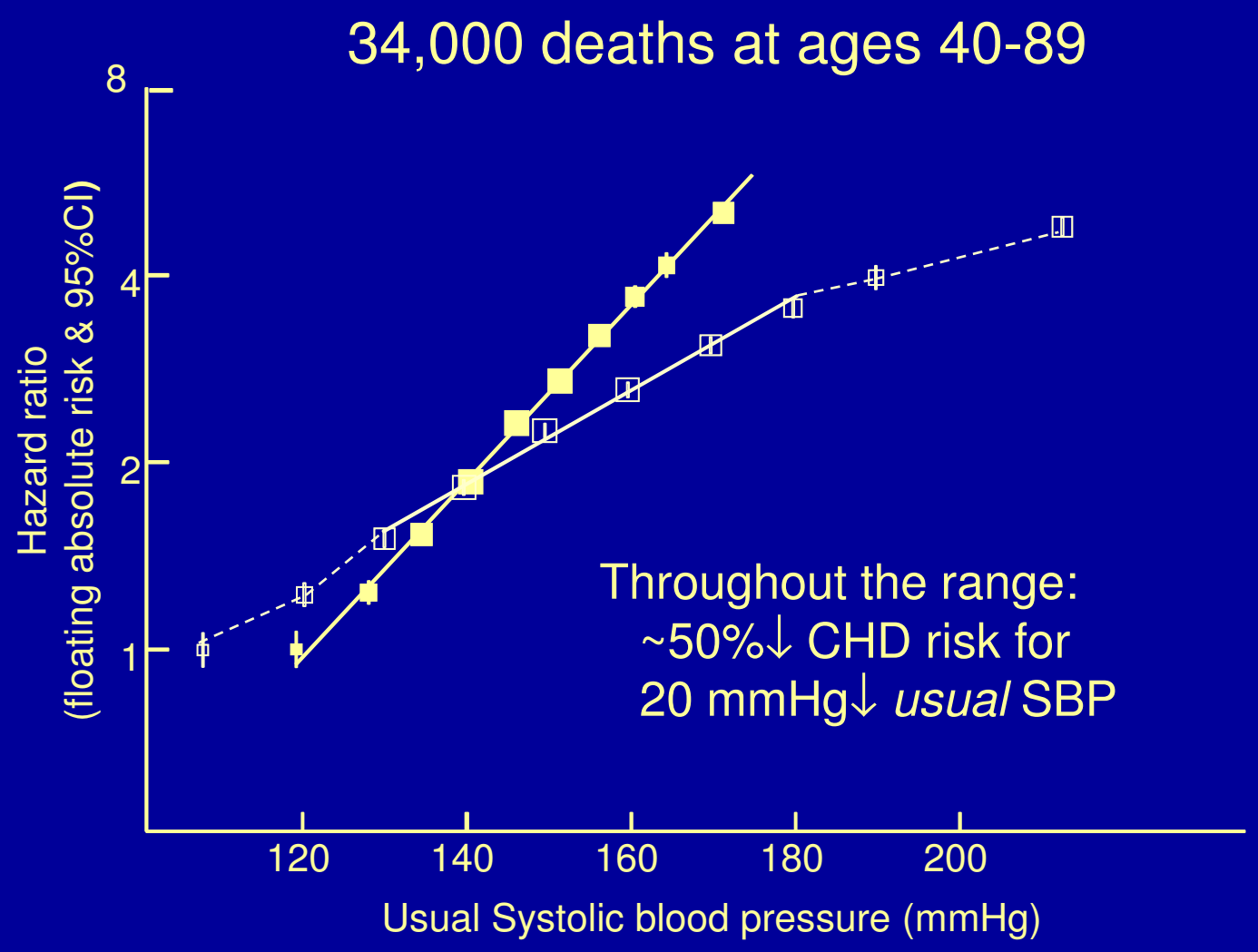
Prospective Studies Collaboration (PSC): CHD mortality versus baseline SBP

34 000 deaths at ages 40-89



Between 130-180 mmHg:
~25%↓ CHD risk for
20 mmHg↓ *baseline* SBP

PSC: CHD mortality versus usual SBP



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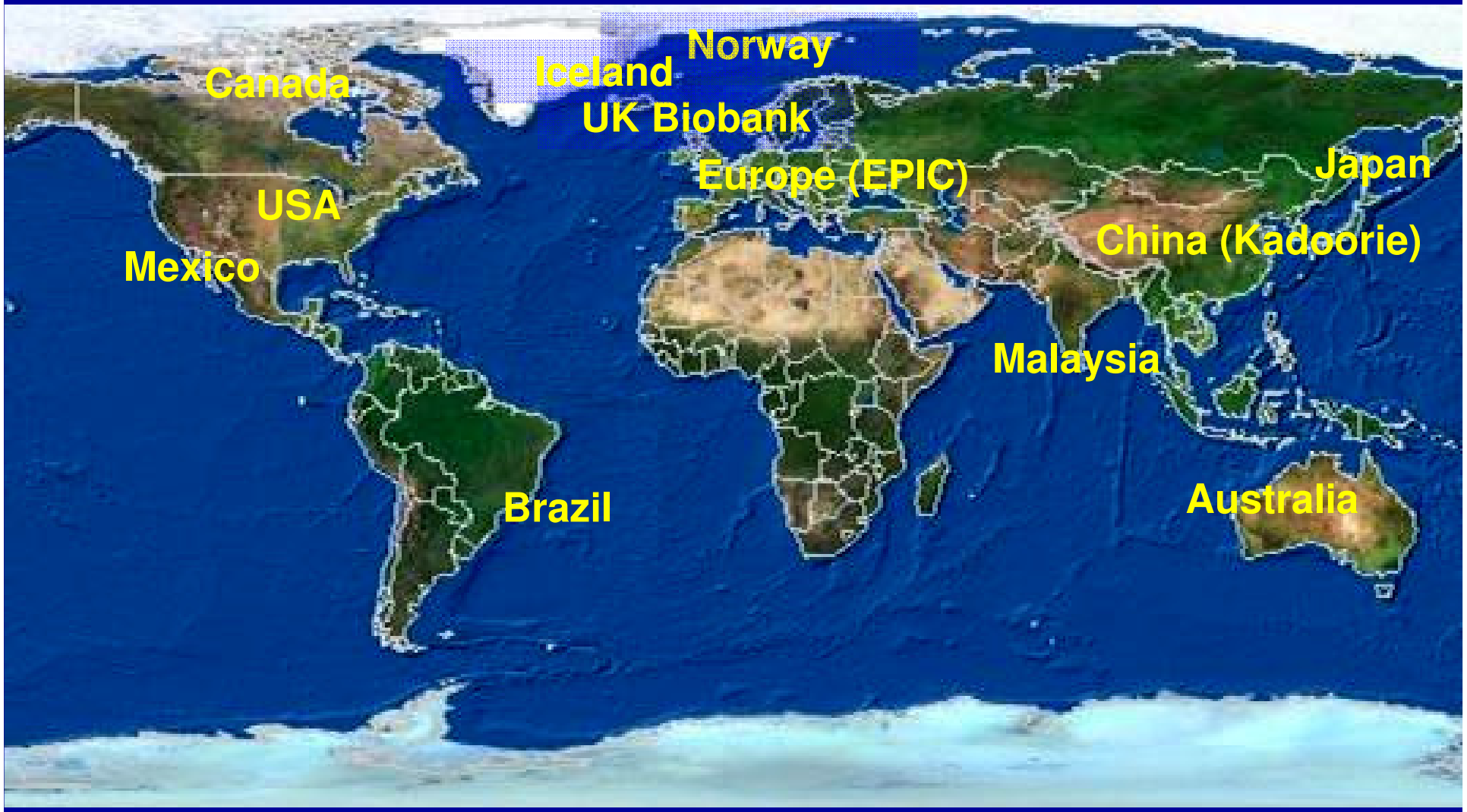

Kadoorie Biobank Study of 0.5M adults

Chinese CDC/CAPM, Beijing
CTSU, University of Oxford, UK