

II. DETAILS OF PROPOSED RESEARCH

Detailed outline of proposed research (see notes attached for further details).

1.0 BENEFITS TO THE NHS

The British Regional Heart Study (BRHS) has provided important information on the causes and natural history of cardiovascular diseases among a nationally representative sample of middle-aged British men. However, its value has always been limited by its exclusion of women. The present proposal provides an opportunity to rectify this by recruiting a parallel cohort of 4400 women of the same age (59-79 years) and from the same 24 towns as the existing cohort of men.

There is a pressing need for information on the distribution of cardiovascular diseases and cardiovascular risk factors in British women, and the use of health services in relationship to need¹. Much of the existing work has been carried out in men, and its direct extrapolation to women is not necessarily justified. Although the sample size is smaller than the original male cohort, the increased disease rates at older ages will provide sufficient statistical power for precise estimates of relative risk within a short time.

The extended framework will provide benefits to the NHS in the following areas:-

1.1 Cardiovascular morbidity: prevalence, incidence and disability. Morbidity and disability data will augment routine mortality statistics providing information of more direct relevance to health care and prevention. This data would also aid understanding of the causes of social and geographic variation in cardiovascular disease risk which is an essential first step in developing policies to reduce inequalities in health.

1.2 Risk factors for cardiovascular disease. Information on risk factors for cardiovascular disease and their interactions will help to clarify the effects of unemployment, physical inactivity, obesity, alcohol use, diet and smoking on women's risk of cardiovascular diseases. New data will also enable risk factor scoring systems for women, comparable to those promoted in men, to be developed for use in primary care. Monitoring of changes in cardiovascular risk factors, regional and male/female variation in trends will also be feasible and will complement information obtained from the Health Survey for England.

1.3 Investigation and treatment of cardiovascular disease

There has been considerable concern about the limited extent of investigation and treatment of coronary heart disease in women. Variation (by age, sex, social class, and region) in investigation and treatment rates, with due allowance made for disease severity, would be examined.

2. VALUE OF THE BRITISH REGIONAL HEART STUDY TO POLICY MAKERS

2.1 National, comprehensive information. The British Regional Heart Study has an impressive track record for providing relevant and authoritative information on the distribution of cardiovascular diseases and their risk factors, the causes of cardiovascular diseases and the relationships between disease and health services. Routine mortality statistics and the Health

Survey for England do not provide policy makers with the detail required to give a coherent response to questions of public importance. Information covering the whole of Britain and derived from an independent on-going cohort study is much less likely to be dismissed as pertaining to only a part of the country or as out of date.

2.2 Testing new hypotheses efficiently. The BRHS has demonstrated its ability to tackle questions of current topical relevance speedily. For example, concerns raised by case-control studies that *Helicobacter pylori* was an independent cause of coronary heart disease have been shown to be due predominantly to confounding by smoking and social class which has avoided the need to set up new cohort or intervention studies to assess the potentially very large policy implications.

2.3 Health of the Nation: secular and geographic trends. Secular trends in cardiovascular mortality rates show marked variation between different parts of the country and between socio-economic groups. Both incidence rates and case-fatality are falling with time, but their relative contribution to mortality rates by region or social class is not clear. Unravelling the causes of secular and geographic trends is of basic importance in setting appropriate targets for monitoring national health policy.

2.4 Clinical guidelines. The British Regional Heart Study is an important resource to draw upon in the preparation of clinical guidelines and training materials on risk evaluation, primary and secondary prevention for cardiovascular diseases.

3.0 BACKGROUND OF THE PROJECT

3.1 Cardiovascular disease in women.

Although incidence and mortality rates from ischaemic heart disease and stroke are lower in women than in men, they are the leading cause of death in women in Great Britain, accounting for over a third (35%) of deaths at all ages in 1994². The ratio of male to female mortality rates decreases with increasing age, which may be due to a deceleration in male risk, rather than a loss of protection associated with the menopause in women³. Coronary heart disease death rates in British women are higher than those in Italian and Greek men and ten times higher than those in Japanese women⁴. Within Great Britain there are marked regional differences in coronary heart disease mortality, with the lowest rates in South Eastern England and the highest in Northern England, South Wales and Scotland - a similar distribution to that in men⁴. These facts suggest that a substantial proportion of mortality is avoidable.

There is little information available on the prevalence of different manifestations, particularly angina, and disability due to coronary heart disease and stroke in British women. Cardiovascular disease appears to be a major cause of disabled life expectancy⁵.

3.2 Risk factors in women. The reasons for the differences in coronary disease risk between men and women remain uncertain⁶, as differences in CVD rates are not explained by variations in major risk factors⁷. Prospective studies have shown that the major risk factors are of importance in women, but relative risks are generally lower, although the prevalence of some modifiable risk factors is higher in women. A summary of these findings is shown in the table.

Risk factor	Sex differences
Smoking ⁸⁻¹²	Similar or greater effect in women than men. Stopping smoking associated with declines in disease risk. Increased prevalence of smoking in younger women
Blood pressure ¹³⁻¹⁵	Similar effect in women and men. Increased prevalence of systolic hypertension in older (ie. 65+) women. Geographic gradient of blood pressure.
Blood cholesterol ^{16,17}	Similar effect of total cholesterol in women <65 years, but greater attenuation of risk among 65+ years. Protective effects of HDL-cholesterol apparent in both older and younger women, but not older men.
Physical inactivity ¹⁸	Inconsistent findings on independent role of exercise in women. Prevalence of inactivity very high among older women.
Obesity and waist- hip ratio ¹⁹⁻²⁵	Increased risk of CHD among obese women, but confounded by other risk factors (diabetes, lipids, hypertension). Waist:hip ratio is a better predictor of CHD risk in both men and women. Role of weight loss not clear in either men or women.
Diabetes ²⁶⁻²⁹	Greater risk of CHD among diabetic women than men. Diabetes commoner in women than men.
Alcohol ³⁰	Relationships with CHD uncertain.
Social class ³¹⁻³³	Women's social class gradients similar or greater to those in men.
Menopause and hormone replacement therapy ³⁴⁻³⁹	Younger age at menopause associated with increased CHD risk. Use of HRT associated with reductions in risk of about 40% but possibility of confounding and bias in selection for treatment. Low prevalence of use in Britain.
Fibrinogen, factor VII ⁴⁰⁻⁴³	Similar effects in men and women. Levels of fibrinogen and factor VII are higher in women than men, and increase post-menopausally

Few British prospective studies are able to examine the reasons for sex differences in cardiovascular diseases, particularly at older ages where disease rates are high. Much of what is known comes from the Renfrew and Paisley Study⁴⁴, the Scottish Heart Health Study^{45,46} (both based in Scotland), and the Whitehall II Study⁴⁷, based on an occupational cohort and confined to London.

Despite considerable work on risk factors in women, there is controversy over the role of several potentially modifiable risk factors in women: alcohol use; HDL-cholesterol in older women; physical inactivity; obesity and waist:hip ratio; fibrinogen; social class. The stronger relationship between diabetes and coronary heart disease among women than men²⁶, and the more consistent relationships between obesity and coronary heart disease in women^{19,20}, suggest that the insulin resistance syndrome may have a fundamental aetiological role in women.

A new, large-scale, comprehensive and nationally representative study is needed among British women to clarify the role of these major risk factors.

Newer risk factors, particularly genetic factors⁴⁸, hyperhomocysteinaemia⁴⁹, haemostatic factors⁴³, dietary antioxidant intake⁵⁰, dietary trans fatty acid intake⁵¹ also require systematic and comprehensive study among women. Variation in such risk factors, and interactions with the major CVD risk factors, may play a part in the marked - and unexplained - social class and geographic variation in cardiovascular disease in Great Britain and are therefore of considerable concern as several of them are potentially modifiable.

The aetiological role of these new risk factors compared with conventional risk factors is unclear. New nationally representative data would be helpful in clarifying relationships in an effort to develop better health policies on diet and exercise.

3.3 Identifying women at high risk of cardiovascular diseases. The development of multiple risk factor scoring systems for the identification of subjects at high risk of cardiovascular diseases⁵²⁻⁵⁵ provides a means of more accurate targeting of health promotion in primary care. However, these systems have been validated exclusively in male populations. Development and testing of such systems in women is therefore of considerable importance.

3.4 Investigation and treatment of cardiovascular diseases in women Women with comparable symptoms to those in men are thought to be less likely to receive coronary angiography⁵⁶⁻⁵⁸, may be less likely to undergo coronary revascularization than men⁵⁹, or attend cardiac rehabilitation programmes after a clinical event⁶⁰. It is possible that the relative exclusion of women from randomized controlled trials of these interventions explains their limited access to treatment⁶¹. These variations in access to care require further examination in a nationally representative British cohort of women.

3.5 The British Regional Heart Study (BRHS). The proposed study in women will use the structure and methods of the BRHS. The BRHS is a unique national prospective investigation into the fundamental causes of cardiovascular diseases in men^{62,63}. In 1978-80, 7735 men aged 40-59 were drawn at random from one general practice in each of 24 towns in England, Wales and Scotland and had a detailed assessment including a questionnaire on personal and family factors, an electrocardiogram, lung function tests and a blood sample for 24 biochemical and haematological measurements. Serum from men in 18 towns was deep frozen (-20°C) for later studies.

The existing programme of BRHS work is funded by programme grants from the British Heart Foundation and the Department of Health until the end of 1999. The core team will provide support in setting up the study.

3.6 New field study in men. Additional funding has been obtained for a further independent field study of the existing cohort of men. This work is now at an advanced stage and training of nursing staff will start in January 1998 and the first field visit will be in Harrogate, starting on February 16th, 1998 and lasting for two weeks. The rolling programme of field visits will be completed by December 20th, 1999. It will be feasible to incorporate concurrent field visits for surveys of both men and women from August 1998.

Strengths of the study Post-menopausal women are at high absolute risk of cardiovascular disease, and the aetiological importance of modifiable risk factors at this age is of great relevance to the development of better methods of prevention. The proposed study design will permit standardized comparisons of men and women of similar ages throughout Great Britain. This would permit differences in disease occurrence, risk factor profiles, and use of health services to be identified. The new study will use the tried and tested methods of the BRHS which gives representative, national coverage, completeness of follow up, with only 21 (0.3%) of the original male cohort unaccounted for, and at least 90% responding to postal questionnaires. The NHS Central Registry tagging has provided complete ascertainment of mortality for those men still resident in the UK. The regular two-yearly medical record review has provided an efficient and accurate means of identifying non-fatal cardiovascular events and new diagnoses of diabetes and angina. The study has never attempted to influence clinical

practice of the participating general practitioners, and remains purely observational, and is therefore capable of generalisation to primary care throughout the country.

4.0 PLAN OF INVESTIGATION

The new study will be based on the 22 British towns in the British Regional Heart Study framework but will exclude Dewsbury and Maidstone which were included in a recently completed pilot study (see below). It is intended to recruit an age-matched parallel cohort of women from each of the 22 general practices in the framework. A total of 200 women per practice will be included, giving a target recruitment of 4400 participants.

4.1 Objectives

- a. To describe in British women the prevalence of symptoms, diagnoses, and disability associated with coronary heart disease, stroke, peripheral arterial disease, and heart failure by age, social class, and geographic region.
- b. To describe in British women, the levels of risk factors for cardiovascular disease, their inter-relationships, and associations with prevalent cardiovascular disease by age, social class and geographic region.
- c. To examine variation in patterns of use (ie. by age, social class and geographic region) of preventive, primary and secondary health services for cardiovascular disease in British women.
- d. To compare the prevalence of cardiovascular disease, risk factor levels, and management of BRHS men and women.
- e. To establish follow up methods for analyses of the relationships between risk factors and cardiovascular disease incidence in older women.

4.2. Sampling and invitation procedures In order to recruit a cohort of 4400 women, a random sample of 6000 women will be drawn from the age-sex register of the 22 study Practices (75% response rate assumed). Sampling will be stratified by town and by 5-year age-group to ensure that the distribution of the cohort of women is proportionately matched by town and age with that of men. The original General Practice or a Health Clinic in the town will be used as the survey base where possible. Transport will be arranged for frail or disabled subjects. It will be possible to plan field work for both men and women in the same towns from August 1998 which will permit 16 towns to have concurrent measurements. Prior to this time, field site arrangements have already been made for men only. The women's field study team will work independently of the men's team but will make use of the same field survey planning processes organised by the core team.

4.2.2 Assessment procedures All assessments will be carried out by a team of three fully trained survey nurses. They will visit each town in turn, following the same order as in the earlier survey which ensured that towns with similar geographic and mortality characteristics were not examined together. The assessments made will include:-

- a. An interviewer-administered questionnaire

Measures of current cardiovascular disease status A modified WHO (Rose) chest pain questionnaire, enquiring about symptoms of angina and possible myocardial infarction⁶⁴; questions about symptoms of intermittent claudication and heart failure; previous doctor diagnoses of cardiovascular disease and diabetes; questions about physical disability, handicap and their cause. Risk factors. Enquiry will be made about a wide range of risk factors: smoking, alcohol consumption, dietary intake of relevant foods (fish, dairy and other fats, fruit and vegetables, vitamins - including supplements), social factors (occupation, retirement, income, support), physical activity, family history of disease, use of medication. Questions about changes in cigarette smoking, alcohol intake, physical activity, employment status, and retirement (type, age of event, activities since retirement) will also be asked. Information will be sought on timing of menopause; premenopausal and post-menopausal history of hormone use (replacement and contraceptive).

Investigation and management for cardiovascular disease History of previous investigation for cardiovascular disease and levels of cardiac symptoms at the time; record of previous and present treatment, medical and surgical (NHS and private); previous and present medications (prescribed and over-the-counter).

b. Physical measurements Standardized measurements of height, weight, waist and hip circumference, blood pressure and lung function (spirometry) will be made. Room temperature will be measured at the time of each subject's measurements.

c. Other assessments

A resting electrocardiogram for computerized analysis⁶⁵ will be carried out (Professor PW Macfarlane, Glasgow).

A fasting venous blood sample will be taken for measurements of total serum cholesterol, lipid fractions, glucose and insulin. Citrated plasma samples will be taken for measurement of fibrinogen and Factor VII (Prof G. Lowe); samples will also be prepared for antioxidant vitamin analysis (Prof A.F. Winder, London). White cell samples (in EDTA) will be set aside for genetic studies (Professor S.E. Humphries, London); additional serum and plasma samples will be held for later analyses. All samples will be centrifuged, separated and frozen within 8 hours, and transferred for storage at -70°C; in the case of haemostatic factors separation and snap freezing on dry ice will be carried out within 2 hours.

Medical record studies With the permission of participants, hospital referrals for cardiovascular disease will be followed up by review of hospital records to document the extent of investigation and treatment.

4.2.3 Follow-up The women will be 'tagged' at the National Health Service Central Register, so that death notification, death certificates and cancer registrations are automatically provided in the same way as for men. The women will be followed up for cardiovascular morbidity using the biennial General Practice review, in precisely the same way as in the study men.

In addition, new cases of acute heart failure will be documented, using standard diagnostic criteria⁶⁶.

4.3.4 Standardization of measurements

A range of methods will be used to ensure reliable information is obtained.

- * full training and standardization of observers, with monitoring of inter-observer variability;
- * the use of a validated automated blood pressure recorder (Dinamap 1846)⁶⁷ and spirometer (Vitalograph Compact), both of which can be calibrated regularly during the study;
- * fully standardized laboratory methods will be used. Laboratory-blinded split samples will be used both to examine within-town and between-town variability.

4.4 Main analyses proposed

4.4.1 Analyses on risk factors, disease prevalence and management

Risk factor distribution The levels and distributions of cardiovascular risk factors in the study population and their inter-relationships will be examined; differences between age groups, social class groups and region will be identified.

Prevalence of cardiovascular disease The rates of specific manifestations of cardiovascular diseases and disability will be examined; differences between age groups, social class groups and region will be identified.

Investigation and treatment of cardiovascular diseases Variation in investigation and treatment of cardiovascular diseases will be examined. Differences in rate and extent of investigation between age-groups, socio-economic groups and geographic region will be examined, taking into account the severity of symptoms at the time of referral.

Comparisons with BRHS men The cohort of women will be of comparable age with the men and will have had measurements made concurrently with men in 16 of the 22 towns. Information derived from postal questionnaires and medical record reviews will be used to examine differences between men and women in risk factors, prevalence of disease, and management.

4.5 Sample size considerations

4.5.1 Risk factor levels between towns. The inclusion of 4400 women will allow comparisons of risk factor levels at the town level based on approximately 200 women. Such numbers will allow the mean systolic blood pressure for each town to be estimated to within 2.5mmHg of its true mean (with 95% confidence) assuming a between subject standard deviation of 18mmHg. Similarly, total blood cholesterol would be estimated to within 0.2mmol/l of its true value (with 95% confidence) assuming a between-subject sd of 1.5mmol/l.

4.5.2 Prevalent cardiovascular disease between towns Prevalence of angina, for example, is expected to be about 5-7% at this age (59-79 years)⁴. The sample size of 200 women in each town would be sufficient to detect with 80% power at the 5% significance level, a 2.5 fold difference in prevalence between towns and a 1.5 fold difference in prevalence between five major geographic regions in England.

4.5.3 Incidence of major cardiovascular disease events. While the main focus of this proposal is on cross-sectional comparisons, the proposed sample size will be adequate for prospective examination as major coronary event rates are rising in this ageing cohort. During the first three years of follow-up, more than 200 major cardiovascular events (including fatal and non-fatal myocardial infarction and stroke) would be expected among 4400 women on the basis of England and Wales mortality statistics and case-fatality rates. The relations of risk factors measured in this new survey to cardiovascular outcomes can therefore be examined at an early stage of follow-up.

4.5.4 Variation in use of health services between towns. Assuming an investigation, referral or treatment rate of 30%, the sample size of 200 women in each town would be sufficient to detect with 80% power at the 5% significance level, a 1.5 fold difference in investigation, referral or treatment rates between towns.

4.6 Pilot study

During February to April 1996, detailed pilot studies were conducted in Dewsbury (high cardiovascular disease risk town) and Maidstone (low risk town). All procedures described above were used. A total of 200 women were examined in each town over a period of two weeks. A response rate of 81% to the postal questionnaire was obtained and 68% completed all the physical measurements.

4.6.1 Training and pilot study The nurses will undergo training in questionnaire administration, physical measurements and other procedures before the study begins. High degrees of between- and within-observer agreement in measurements will be ensured before fieldwork begins. Retraining will be carried out at intervals through the study. Full scale pilot studies in two towns (Dewsbury and Maidstone) have recently been completed (see above). Nurses recruited for the new study of women will pilot the methods in Peterborough which was used as a pilot site for the original study.

4.6.2 Timetable Three months will be required for protocol development, staff recruitment, and to visit all Practices to provide orientation for the new study. Full training of the field team and completion of pilot studies will also take three months (June 1998 to August 1998). The survey of women in each town (approx. 200 women in each town) will take two weeks, with two weeks' preparation time between each survey visit. The 22 town visits will be completed within 26 months (August 1988 to Sept 2000) with allowance for holidays. Data cleaning and preliminary analyses will be carried out between November and December 2000. The main analyses and reports on the new data will be completed during the following year (January 2001 to June 2001).

4.6.3 Feasibility The British Regional Heart Study Research Group has unparalleled practical experience in the conduct of geographic studies of cardiovascular disease epidemiology both in adults and children. Our pilot study experience has demonstrated both the willingness of women participants and general practices to take part in field work. The General Practice network required for the study is in place and members' interest and enthusiasm for further studies remains high.

4.6.4 Ethical considerations The procedures involved in the present study are similar to those

employed in the earlier BRHS survey in adults and in our recent surveys in children, when they were approved without reservation by local Research Ethics Committees. Ethical approval for the new study will be sought from all relevant local Committees at an early stage.

5.0 PROJECT MILESTONES

5.1 Year 1

- 5.1.1 Development and testing of field survey instruments
- 5.1.2 Sampling frames and selection of participants
- 5.1.3 Recruitment and training of nurse researchers
- 5.1.4 Completion of pilot study

5.2 Year 1 and 2

- 5.2.1 Completion of 22 town surveys
- 5.2.2 Coding and cleaning of data from new survey completed

5.3 Year 3

- 5.3.1 Analyses and reports completed.

6.0 DISSEMINATION AND IMPLEMENTATION OF FINDINGS

The British Regional Heart Study has an excellent track record of publications of relevance to both policy and clinical (both medical and nursing) practice. A six-monthly newsletter is produced and is circulated (and read) widely. All key publications have been circulated to the Department of Health and other agencies. Locally relevant information (eg. local risk factor profiles) has been sent to regional and local Health Authorities. The York Centre for Reviews and Dissemination and proposed NHS Implementation Centre provide new means of dissemination. Links are already established with the York Centre and early discussions will be held with Professor Andy Haines, Chair, NHS Implementation of Research Findings Committee about how this work may be used. The BRHS will be an important resource to draw upon in the preparation of clinical guidelines and training materials on risk evaluation, primary and secondary prevention for cardiovascular diseases. Implementation of findings will be largely at the level of guiding national policy on the balance between primary and secondary care for the prevention, investigation and treatment of cardiovascular diseases.

The BRHS is well-known in scientific and policy circles and is frequently approached for advice, use of data for specific purposes (eg. meta-analyses of cholesterol and cardiovascular disease, weight change and cardiovascular disease) and is viewed as a national resource in this field. Consequently, material derived from the BRHS has an authority that derives from the integrity of the study design and its successful track record.

7.0 JUSTIFICATION FOR SUPPORT REQUESTED

A total of ,742,170 is sought to carry out this work, of which ,460,110 comprises staff salaries and the remainder is for field work and equipment. Costs for field work have been broken down to give nominal prices per subject of ,115 and per town of ,23,000.

7.1 STAFF

7.1 The British Regional Heart Study `Core Team'

Expert guidance and support for the study will be provided by the existing British Regional Heart Study Research Group, including the co-applicants and the core team, the study coordinator, Mrs Mary Walker, and Mr Andy Thomson (Computer Programmer) both of whom are funded to the end of 1999. The requirements for carrying out the new study are:

7.1.2 Study Coordinator Preparation for a new study will require a study coordinator with specific responsibility for the smooth running of the women's study throughout the whole field study. A full time coordinator is sought for this work for three years.

7.1.2 Research Nurses Three Research Nurses (as in the previous BRHS field work) will be required to carry out assessments in the new survey, which include physical measurements, a resting ECG, and blood taking. Nurses will only be asked to check completeness of previously circulated postal questionnaires which will reduce their work load considerably. Allowing for training, pilot study and the full survey, employment for a 30 month period will be required.

7.1.3 Computer programmer A junior computer programmer would play an essential role in preparation of invitations, examination materials, in supervising data entry and cleaning during the course of the study. A full-time post for three years will be required.

7.2 EXPENSES

7.2.1 Visits by investigator and research coordinator. A visit will be made to each practice in preparation for the field work and funds are also required for one supervisory visit per survey site during the field work. Travel and accommodation costs will be required for these visits.

7.2.2 Practice co-ordinator liaison Practice Co-ordinators (often the receptionist or Practice Manager) will be involved in coordinating invitations and appointments for the new survey and acting as a receptionist during the field work. A total of ,11,880 (,540 for each of 22 coordinators) is required to cover these costs.

7.2.3 Postage, printing and communications A sum of ,3 per participant invited is required to cover these costs.

7.2.4 Travel and accommodation for the main survey A Transit Van will be hired for each two week survey period to move staff and equipment to the survey site (,650 per town). An allowance for van hire and petrol is requested. Accommodation and a subsistence allowance (combined estimate ,70/day/person) to cover the two-week field survey period in each town is requested.

7.2.5 Patient travel An allowance is requested to cover the cost of travel of frail or disabled participants to examination centres.

7.2.6 Blood sampling and basic analyses An allowance of ,4.50 per subject is requested to

cover the costs of equipment for blood sampling and collection and ,17.50 to cover the cost of basic biochemical analyses (total cholesterol and lipid fractions, blood glucose, insulin). Support for the more complex and costly analyses (antioxidant vitamins, coagulation factors, genetic analyses) will form the basis of separate applications.

7.2.7 Electrocardiographic tracing analysis Computerized interpretation of the ECG recordings (Prof Peter Macfarlane, Glasgow) will cost ,7 per subject.

7.2.8 National Health Service Central Register tagging Support is requested for `tagging' of women at the NHS Central Register, to provide information on date and cause of death. In order to study the representativeness of participants, and the bias introduced by non-participation, this request is extended to cover the costs of `tagging' non-participants (estimated at 1500 of 6000 invited).

7.2.9 Data entry Costs of data entry are estimated at ,3 per completed data set per participant.

7.3 EQUIPMENT

An automated ECG machine, the Siemens Sicard Portable 460, together with cables, modem and disposable electrodes. A request is also made for a freezer (11.5 cubic feet, -70°C) to provide storage for samples being held for later analyses. One automated blood pressure monitor and one portable spirometer will be required. All other field equipment (centrifuges, couches, stadiometers, scales, electronic pipette-aids, portable field-freezers) will be provided by the study department.

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