



WORLD HEALTH ORGANIZATION
 ORGANISATION MONDIALE DE LA SANTÉ

*mass screening
 data collection
 cvd - P²c*

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Joint Aq/Kuro Projection

MULTINATIONAL MONITORING OF TRENDS AND DETERMINANTS
 IN CARDIOVASCULAR DISEASES

INDEXED

"MONICA PROJECT"

MANUAL OF OPERATIONS



PREFACE

This Manual of Operations is designed to complement the Proposal and Provisional Protocol for the Monica Project.* Whereas the protocol introduced and described the project in general terms, the Manual of Operations is designed for those who are going to put it into effect. The Monica Project has many facets and the Manual will inevitably need to be revised, amended and corrected, particularly in the early stages. Particular sections will be of interest to certain members only of the Monica team. They may be needed in the field and will be supplemented by local instructions. For these reasons the Manual will be distributed in sections in loose leaf form and each section will be dated with the date of its last revision. Revisions of specific sections can by this means be issued without producing a new edition of the whole manual. With each revision a new dated list of contents will be issued so that the collaborating centres can check that their manuals are up to date, but they will be responsible for substituting the revisions into their own copies. Each centre will need only a small number of Manuals but may request extra copies of specific sections.

Each centre will need to prepare its own Manual of Operations based on this document. Two model manuals are being circulated with it as examples: the Minneapolis and Finnish Manuals. Each Centre will need to submit its own manual, translated into English, to the coordinating centre for approval in due course. It is important that methods do not vary too much between centres and also that operations are specified within centres so that techniques do not change over time in an uncontrolled manner.

* For a discussion of the background and rationale of the project, refer to the Proposal and Protocol (document WHO/MNC/82.1).

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SECTION 1:

Objectives, Design and Hypotheses

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SECTION 1 - OBJECTIVES, DESIGN AND HYPOTHESES (see also Protocol)

- 1.1 Main objective: "To measure the trends in cardiovascular mortality and coronary heart disease and cerebrovascular disease morbidity and to assess the extent to which these trends are related to changes in known risk factors, daily living habits, health care, or major socio-economic features measured at the same time in defined communities in different countries".

Specifically, this means mounting feasibility and pilot studies during 1982 and beginning a ten year monitoring programme in 1983.

- 1.2 Subsidiary objectives: These are needed to accomplish the main objective.

- 1.3 Target population: To define within each area a suitable population on which full demographic and socio-economic data can be obtained from the National Census before the start and near the finish of the study period (of ten years) with the possibility of making intercensal annual estimates of population change. The target population is that which qualifies as being at risk for cardiovascular events and as the sampling frame from which individuals may be drawn for screening and to answer questionnaires.

1. Mortality measurement: To obtain complete death certificate data on subjects aged 25-64 years from the above populations, who die during the study period, tabulated by five year age groups and by cause, coded by the normal routine procedure (ICD - 4-digit codes, 3-digit, A series or major disease categories).
2. Coronary events: To record all fatal and non-fatal recognized coronary events that satisfy the study criteria in subjects aged 25-64 years from the at-risk-populations which occur during the study period. (False positive cases - those so diagnosed clinically which do not qualify will also be recorded to study trends in diagnosis).
3. Stroke events: To record all fatal and non-fatal recognized stroke events that satisfy the study criteria in subjects aged 25-64 years from the at-risk-populations which occur during the study period. (False positive cases - those so diagnosed clinically which do not qualify, will also be recorded to study trends in diagnosis).
4. Risk factors: To measure at three points during the study period levels of cardiovascular risk factors and self-reported health knowledge and behaviour in samples of subjects drawn from the at-risk-population. The essential risk factors are
 - Smoking
 - Blood pressure
 - Serum cholesterol
 - Weight and height (expressed as body mass index).
5. Health care: To monitor the nature and change in medical care of coronary and stroke events, both in treatment of acute events and in secondary prevention, i.e.:
 - Acute hospital and mobile coronary care
 - Home versus hospital management
 - Anti-arrhythmic and beta blocker usage
 - Long-term treatment of angina and hypertension
 - Systematic rehabilitation programmes
 - Coronary artery and carotid artery surgery
 - Diagnostic procedures.

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SECTION 2:
Organization, Management and Policy Concerns

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SECTION 3:

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SECTION 3 - ELIGIBILITY AND EXCLUSION CRITERIA

3.1 Coronary events

To qualify as an event for the core study:

- a) The subject must be a resident of the target area aged between 25 and 64 years when the event occurred;
- b) The event must have had its apparent onset within the study period and more than 28 days from any preceding recorded coronary event in the subject;
- c) The event must satisfy the criteria for Definite or Possible Myocardial Infarction or, if fatal, must satisfy these criteria or those for death from coronary heart disease;
- d) The event must have been detected and diagnosed within 28 days of onset.

The core study is not concerned with nonfatal events initially treated as possible coronary events but eventually diagnosed as something else. (These cases were coded as "Not Myocardial Infarction" in the WHO Myocardial Infarction Registers). However, the core study is concerned with "false positives", that is cases diagnosed clinically as coronary events but classified by the centre concerned as something else. The trends in "false positives" and in those false negatives detected by study of related clinical diagnoses of deaths and hospital discharges will constitute an important source of data in the analysis of the trends in fatal and nonfatal attacks that satisfy the study criteria.

Each centre will need to carry out a pilot study to determine the best local sources of cases and, in the case of hospital discharges, to discover the diagnoses or ICD code numbers that yield cases satisfying study criteria for coronary events. Once sources and ICD codes have been determined it is important that methods are not changed over time without measuring the consequences, as a change of sources may cause a spurious change in event rates.

It is presumed that all diagnoses of myocardial infarction and acute coronary insufficiency will be followed up as well as symptomatic diagnoses such as chest pain or cardiac arrest. Unlike the death certificate diagnoses of hypertension and chronic ischaemic heart disease, these diagnoses in nonfatal cases may be found to be unproductive but should be examined in the pilot study.

Periodically during the 10-year period a random or stratified sampling of hospital cases should be done to search for changes in the pattern of cases.

Where multiple field discharge data are available a different set of rules may be applied for main and subsidiary diagnoses.

For cases outside hospital for which no ICD coding has been done at the time of notification, diagnoses such as myocardial infarction, cardiac infarction, coronary thrombosis, coronary insufficiency, heart attack, will need to be reviewed.

3.2 Stroke

To qualify as an event for the core study

- a) The subject must be a resident of the target area aged between 25 and 64 when the event occurred;
- b) The event must have had its apparent onset within the study period and more than 28 days from a coronary event which takes precedence;
- c) The event must satisfy the criteria for cerebrovascular stroke;
- d) The event must have been detected and diagnosed within 28 days of onset.

The core study is not concerned with cases initially treated as possible strokes but eventually diagnosed as something else. However, the core study is concerned with "false positives", that is cases diagnosed clinically as stroke, but classified by the centre as something else. The trends in "false positives" and in those false negatives detected by study of related clinical diagnoses of death and hospital discharges will constitute an important source of data in the analysis of the trends in fatal and nonfatal attacks that satisfy the study criteria.

Each centre will need to carry out a pilot study to determine the best local sources of cases and, in the case of hospital discharges, to discover the diagnoses or ICD code numbers that yield cases satisfying study criteria for cerebrovascular stroke events. Once sources and ICD codes have been determined it is important that the methods are not changed over time without measuring the consequences, as a change of sources may cause a spurious change in event rates.

For hospital discharges, the diagnoses or ICD codes that yield stroke cases will be 430-434 but 430-438 will need to be reviewed for deaths and for non-fatal cases in the pilot study. Symptomatic diagnoses such as loss of consciousness and generalized diagnoses such as atherosclerosis and hypertensive disease might also be looked at.

For cases outside hospital for which no ICD coding has been done at the time of notification, diagnoses such as stroke, apoplexy, hemiplegia will need to be reviewed.

- 3.3 Residence: In order to qualify as morbidity and mortality events, these must occur in residents of the study area. The definition of a "resident" should be the same as that used in the decennial census in order to calculate event rates. A resident is someone who lives in the study area exclusively or for most of the year (e.g. a student). A visitor would not qualify but someone who has just arrived in the locality and is making a home there would qualify.

Similar criteria apply to eligibility of subjects for screening.

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SECTION 4 - SCREENING FOR RISK FACTORS

The measurement of some risk factors and in particular the three major (serum cholesterol, blood pressure and smoking habits, plus height and weight) in representative samples of the study population is part of the "core study" being integrated in to the questions which the study aims to answer.

Other measurements can be done optionally on a local basis.

Three questions have to be tackled:

- 4.1 Sample size
- 4.2 Sample selection
- 4.3 Frequency of screening.

4.1 Sample size

The statistical calculations shown in Appendix 1b of the protocol as amended in Geneva, October 1982, suggests that 200 subjects are needed in each age and sex group to show the expected changes of risk factor levels, in most situations.

The total sample size should be of 1200 or 1600, depending whether the youngest age group is considered or not (being optional).

| <u>Age</u> | <u>Males</u> | <u>Females</u> |
|--------------|-----------------------|----------------|
| 25-34 | 200 | 200 |
| 35-44 | 200 | 200 |
| 45-54 | 200 | 200 |
| 55-64 | 200 | 200 |
| Total | 800 (or 600) | 800 (or 600) |
| Grand total: | <u>1600 (or 1200)</u> | |

Such estimates start from the assumption of a 100% participation which is definitely unrealistic.

Therefore each centre should estimate the expected participation on the basis of previous experience and/or of a pilot study and enlarge the sample size in proportion. As an example, if 70% is the expected participation rate, 570 individuals from each group are to be enrolled since 400 is 7/10 of 570. The following points should be kept in mind:

- a) in general, within the specified age groups, a lower participation rate may be expected in younger people, and in men as compared with women;
- b) the self selection resulting from low participation rates may introduce biases in the estimate of means and rates.

4.2 Sample selection

Each sample is an independent one. This means that every individual in the community should have the same chance of being selected for the sample at each screening period.

The method of obtaining the population sample will be determined by local considerations, but the objective is to obtain a random sample of residents rather than samples of convenience, chunk samples, occupational groups, etc.

Since the local characteristics of the population may be extremely variable, no universally applicable rules can be given, but only general guide-lines:

The sampling frames can be:

- population registers
- electoral registers
- taxation registers
- post office or commercial registers
- households
- others.

If the ideal situation is to produce a stratified sample including the following strata: age, sex, urban/rural, but other strata could be considered such as seaside, plain, hills and mountains, industrial and rural, etc.

Random sampling should be performed within each single stratum, maintaining the balance between males and females and between the 3 or 4 age groups.

In practice, a pure (or even geographically stratified sample) in a scattered population may pose serious organizational problems for the logists of the screening staff. A reasonable compromise should be found. Cluster sampling is easier for logistic and organizational purposes, but the number of subjects should be increased (usually by at least one third). Advice must be obtained from a local statistician, and the methods and results discussed with the statistician of the coordinating centre.

Once the sample has been drawn a file should be prepared with individual data, for the purpose of subsequent invitation to the screening.

4.3 Frequency of screening

Since a ten-year collection of mortality and morbidity data is planned, it is recommended that screening occurs at the beginning (year 1), at the middle (year 5) and at the end (year 10). However:

1. allowing a time-lag between changes of factors and eventual changes of incidence and mortality, the screening at year 10 might reveal little or no meaning and therefore a screening at year 8 or 9 seems more logical;
2. if the entry screening cannot take place at year 1 because the centre is not able to start screening and monitoring at the same time, the screening can be done at year 2 and 3; then at year 5 and 6; and then at year 8 and 9.

Two years are indicated each time since 1600 or more people to be examined may involved field work lasting longer than a 12 month period. In any case the screening should be repeated over the same season of the year, as was done previously.

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SECTION 5:

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SECTION 5 - PROCEDURES FOR DATA COLLECTION - MORTALITY AND MORBIDITY

5.1 Coding of death certificates to ICD 9th revision

All death certificates for the study area for men and women aged 25 to 64 years inclusive should be collected during the study period. The cause of death should be coded using the International Classification of Diseases, 9th Revision, and a four digit code, or, if that is impossible, a three digit or A-series code or major disease categories. The coding should be done by a nosologist following the standard practice for the country and region concerned to ensure comparability with national coding practice and national mortality statistics. The objective is to obtain data which, as far as possible, have not been influenced by the register team.

5.2 Fatal cases that might be coronary or stroke events

While each centre should attempt to find the death certificate codes both as primary and secondary causes of death that lead to cases of coronary heart attack and stroke satisfying the Monica criteria, the following table sets out the cause of death codes that should be screened at least in the pilot phase.

Deaths for validation

| <u>Cause of death + ICD</u> | <u>Protocol</u> |
|------------------------------------------------------------------|-----------------------------------------------------------|
| Infection + parasites 001-139 | No |
| Neoplasms 140-239 | No |
| Endocrine 240-279 | 250 diabetes, 272 hypolipidaemia 278 obesity, only. |
| Blood, Mental Nervous 280-389 | No |
| Cardiovascular: | |
| Rheumatic 390-398 | No |
| Hypertensive 401-405 | Yes |
| Ischaemic 410-414 | Yes |
| Pulmonary 415-417 | No |
| Other 420-429 | Yes |
| Stroke 430-438 | Yes |
| Arteries, etc 440-459 | 440-447 only |
| Respiratory 460-519 | No |
| Digestive 520-579 | No |
| Genitourinary, skin, musculoskeletal, congenital, etc 580-779 | No |
| Symptoms, etc. 780-799 | 797-799 only |
| Injury, etc. 800-999 | No |

5.2 Fatal Events

1. Death Certificates

- a) Validation of in-hospital cases: These will be based on the hospital record history, ECGs, serum enzyme and death certificate data. In the case that a patient died before adequate data could be collected, the death should be treated as an out-of-hospital death.
- b) Validation of out-of-hospital deaths: All study-area death certificates should be reviewed at least quarterly or semi-annually. Death certificates that are ineligible because the decedent was outside the age range can be excluded immediately, and those deaths that are clearly due to trauma (e.g. contain a sequence of events including accident, homicide or suicide), chronic obstructive pulmonary disease, cancer, cirrhosis of the liver, or rheumatic heart disease without mention of atherosclerotic heart or vascular disease can also be excluded. However, if an atherosclerotic condition is mentioned in the sequence of events or if the cause of death is attributed to one of the conditions listed above, the cause of death should be validated.

Validation is based on any available medical records + medico-legal records and, if necessary (local option) interview of the decedent's next-of-kin or another informant. Medical records for the period within a minimum of 28 days of death should also be examined for information that may elucidate the circumstances leading to the death. The interview should establish the circumstances surrounding the decedent's death.

5.3 Morbidity

1. Case Determination

1.1 Myocardial Infarction

1.1.1 In hospital

As with stroke, it is the experience in some countries that practically all myocardial infarctions are identified as such but that not all cases identified as myocardial infarction meet the WHO criteria for MI. To assure that this is the case in all study centres, it is suggested that each centre start with a range of discharge codes that is broader than 410 and 411 (e.g. codes for chronic ischaemic heart disease and non-ischaemic heart disease, atherosclerosis, pulmonary embolism and other syndromes associated with chest pain) and document that an insignificant proportion of definite myocardial infarction cases are included in these discharge codes. On an ongoing basis, hospital laboratory data on cardiac enzymes and ECGs can be reviewed to be sure that all cases have been detected.

1.1.2 Out-of-hospital

Out-of-hospital myocardial infarction involves the same procedures as detecting out-of-hospital stroke except that cases may also be detected from clinical pathology laboratory records for cardiac enzymes and electrocardiographic laboratory records if these are used in the study centre's area.

1.2 Stroke

1.2.1 In-hospital

It is suggested that in the early phases of data collection each centre collect data on cases drawn from a broad range of discharge codes which might include stroke assigned to another category. Examples of these beyond ICD9 430-438 might include hemiplegia (432), "certain symptoms referable to the nervous system and special senses" (781). Once it has been established that an insignificant proportion of cases discharged without stroke diagnoses are in fact not stroke, case validation can proceed on a much narrower scale (e.g. 430-434). Documentation of the adequacy of this narrower scale should be repeated every two to five years to assure that there has been no change in hospital labelling practice over time.

1.2.2 Out-of-hospital

In communities where patients in the 25-64 age range with stroke are routinely treated in hospital, routine searches outside will not be cost effective, but even where hospital treatment is said to be the norm, this should be confirmed by questioning physicians in the community in the pilot phase. However, in those countries where stroke is treated in the office or the home, contact must be made with physicians and a protocol established to identify and collect data on stroke cases. This procedure could take several forms and might include reviewing charts on a semi-annual basis, providing each office with a log book and a poster reminding them to log all cases of suspected new stroke, or asking the office nurse or assistant to notify the project in the event that a new stroke is identified. Individual protocols should be documented and reviewed by the coordinating centre for the purpose of improving comparability and to develop a detailed protocol for out-of-hospital detection of morbid events.

2. ECG coding

ECG coding should follow the guidelines and methods outlined in "The Minnesota Code Manual: Procedures for Measurement and Classification of Electrocardiographic Findings in Clinical Trials and Population Studies", by R. Prineas, R. Crow and H. Blackburn, published by John Wright - PSG Inc., Customer Service Department, 545 Great Road, PO Box 6, Littleton, Mass., USA, 1982.

Magnifying lenses with a reticule are necessary for Minnesota coding of ECGs and can be ordered at cost price direct from the Minnesota Coding Laboratory at the Laboratory of Physiological Hygiene, School of Public Health, Stadium Gate 27, 611 Beacon St. SE, Minneapolis, Minnesota 55455, USA. For those centres having difficulties with this, arrangements can be made by the coordinating centre at the Cardiovascular Diseases Unit, WHO, Geneva.

5.4 Diagnostic Criteria for Coronary and Stroke Events

1. Symptoms

At the onset of the present attack:

1.1 Typical - when chest pain is present, characterized by:

- (i) duration of more than 20 minutes AND
- (ii) no definite non-cardiac cause.

(Note: other characteristics are used clinically but as these are not always present they cannot be used in a definition).

1.2 Atypical

- (i) one or more of the following
 - Atypical pain
 - Acute left ventricular failure
 - Shock
 - Syncope.

AND

- (ii) the absence of cardiac disease other than ischaemic heart disease

AND

- (iii) no definite non-cardiac cause.

2. Electrocardiogram

The ECG classification will be based on the reading of all records taken in the period following the acute attack and, if available, records taken immediately before.

2.1 Definite ECG

- (A) The development in serial records of a diagnostic Q wave

- AND/OR -

- (B) The evolution of an injury current which lasts more than one day.

(Note: criterion B is included because diagnostic Q waves are already present in the first ECG recording in many cases.).

The interpretation of two or in some cases three ECG records is therefore necessary for the establishment of these categories.

An evolving pattern of changes (appearance or disappearance within lead groups: anterior (V₁-V₅), lateral (I, aVL, V₆); inferior (II, III, aVF) establishes the infarct as acute.

A. Development of Q waves

Progression of Q codes from no Q to equivocal or equivocal to diagnostic codes requires that serial change rules from the Manual of Operations be applied.

- i) No Q or QS code in one ECG record followed by a record with a diagnostic Q or QS code (Minn. code 1-1-1 through 1-2-5 plus 1-2-7).

- OR -

- ii) An equivocal Q or QS code (Minn. code 1-2-8 or any 1-3 code) and no major ST segment depression in one ECG record followed by a record with a diagnostic Q code PLUS a major ST segment depression (Minn. code 4-1 or 4-2)

- OR -

- iii) An equivocal Q finding and no ST segment elevation in one ECG record followed by a record with a diagnostic Q code PLUS an ST segment elevation (Minn. code 9-2).

- OR -

- iv) An equivocal Q finding no major T wave inversion in one ECG record followed by a record with a diagnostic Q code PLUS a major T inversion (Minn. code 5-1 or 5-2).

- OR -

- v) No Q code and neither 4-1 nor 4-2 followed by a record with an equivocal Q code plus a 4-1 or 4.2.

- OR -

- vi) No Q code and no 9-2 followed by a record with an equivocal Q-code plus a 9-2.

- OR -

- vii) No Q code and neither 5-1 nor 5-2 followed by a record with an equivocal Q code plus a 5-1 or a 5-2.

- OR -

B. Evolution of injury current which lasts more than one day.

- viii) An ST segment elevation (Minn. code 9-2) lasting more than one day

AND

T wave progression on three or more records from 5-0 to 5-3 to 5-2 or from 5-3 to 5-2 to 5-1.

2.2 Probable ECG

Evolution of repolarization changes which last more than one day (one or more of the following):

- i) No major ST segment depression in one ECG record and other records with a major ST segment depression (Minn. Code 4-1).
- ii) No ST segment elevation in one ECG record and other records with an ST segment elevation (Minn. Code 9-2).
- iii) No major T wave inversion in one ECG code and other records with a major T wave inversion (Minn. Code 5-1 or 5-2).

2.3 Non-evolving (ischaemic) ECG

i) Minnesota code 1-1-1 to 1-2-5 or 1-2-7 for Q and QS patterns

- OR -

ii) Minnesota code 9-2 for ST segment elevation PLUS any T wave depression item coded 5-1 or 5-2.

- OR -

iii) Q and QS pattern 1-2-8 through 1-3-6

OR

iv) ST junction (J) and segment depression 4-1 through 4-3.

OR

v) T-wave items 5-1 through 5-3

- OR -

vi) ST segment elevation item 9-2.

2.4 Other ECG

i) All other ECG findings including normal ECG.

2.5 Uncodable ECG

2.6 ECG absent

3. Cardiac enzymes

Appropriate serum cardiac enzyme tests will be used whenever possible. Owing to differing local laboratory circumstances it will not be possible for this study to standardise the serum enzyme tests nor the reagents and methods employed. Each centre should, in cooperation with each local laboratory, define (1) the tests employed, and (2) local ranges of normal, equivocal and abnormal.

Abnormal: At least one serum enzyme level is more than twice the limits of normal when measured within 72 hours of onset of symptoms or admission.

Equivocal: Serum enzyme levels are raised but to less than twice the upper limit of normal.

Non-specific: Serum enzyme levels are raised above normal but there are probable explanations other than cardiac infarction, such as liver disease, infections, defibrillation or surgery.

Incomplete: Tests not done within 72 hours of onset of symptoms or admission.

Normal: Within normal limits.

4. Necropsy findings

The results of post-mortem examination which are recorded in the following section of data requirements for death provide the information for classification into:

Definite evidence of acute myocardial infarction: the presence of a fresh myocardial infarction and/or recent occlusion of a coronary artery (from ante-mortem thrombus, haemorrhage into an atheromatous plaque or embolism). Note that this refers to the naked eye appearance of the heart.

Equivocal: signs of chronic ischaemic heart disease, namely, old myocardial infarction (scar) occlusion or severe stenosis (greater than 50% reduction of lumen) by mural atheroma of one or more coronary arteries in the absence of fatal disease outside the heart.

Negative: (a) the absence of macroscopic evidence of fresh myocardial infarction or recent occlusion of the coronary artery or (b) evidence of fatal disease outside the heart in the presence of chronic ischaemic heart disease.

5. Diagnostic categories

There are the following categories:

- (1) definite acute myocardial infarction
- (2) possible acute myocardial infarction or coronary death
- (3) Ischaemic cardiac arrest with successful resuscitation not fulfilling criteria for definite or possible myocardial infarction
- (4) no acute myocardial infarction or coronary death
- (5) fatal cases with insufficient data.

Allocation of a diagnostic category must follow strictly the definitions provided. The categories used for the diagnosis of "definite" and "possible" acute myocardial infarction are not necessarily those that would be used by a clinician, but rigid definitions are essential for event analysis.

(1) Definite acute myocardial infarction

- (a) Definite ECG or
- (b) Symptoms typical or atypical, together with probable ECG and abnormal enzymes, or
- (c) Symptoms typical and abnormal enzymes with non-evolving (ischaemic), or noncodable ECG or ECG not available, or
- (d) Fatal cases, whether sudden or not, with naked-eye appearance of fresh myocardial infarction and/or recent coronary occlusion found at necropsy.

(2) Possible acute myocardial infarction or coronary death

- (a) Living patients: with typical symptoms, whose ECG and enzyme results do not place them in category (1) and in whom there is no good evidence for another diagnosis for the attack, or
- (b) fatal cases whether sudden or not (not in category 1) where there is no good evidence for another cause of death, clinically or at autopsy:
 - (i) with symptoms, typical or atypical; or
 - (ii) without typical or atypical symptoms, but with evidence of chronic coronary occlusion or stenosis or old myocardial scarring at necropsy; or
 - (iii) with a good history of chronic ischaemic heart disease such as definite or possible myocardial infarction, or coronary insufficiency or angina pectoris in the absence of valvular disease or cardiomyopathy.

- (3) Ischaemic cardiac arrest with successful resuscitation not fulfilling criteria for definite or possible myocardial infarction. Spontaneous cardiac arrest not provoked by medical intervention, electrocution, drowning or other gross physical insults from presumed primary ventricular fibrillation secondary to ischaemic heart disease, in the absence of valvular disease or cardiomyopathy or other serious disease.
- (4) No acute myocardial infarction
- (a) Living patients (not in category (1)):
 - (i) probable, non-evolving, other, uncodable, and absent ECG without typical symptoms or elevated enzymes, or
 - (ii) where illness episode has been explained by another diagnosis.
- (b) Fatal cases, whether sudden or not, not in category (1) where another diagnosis has been made (clinically or at autopsy).
- (5) Fatal cases with insufficient data

Cases with no autopsy, no history of typical or atypical symptoms, no previous history of chronic ischaemic heart disease and no other diagnosis. Living patients should not be allocated to this category. It is hoped that most centres will not need this category.

CEREBROVASCULAR STROKE EVENTS

Definition of stroke

Stroke is defined as rapidly developed clinical signs of focal (or global*) disturbance of cerebral function, lasting more than 24 hours or leading to death, with no apparent cause other than a vascular origin; it includes patients presenting clinical signs and symptoms suggestive of subarachnoid haemorrhage, intracerebral haemorrhage, or cerebral ischaemic necrosis. It does not include transient cerebral ischaemia.

* "Global" - applies to patients with subarachnoid haemorrhage and to some patients in deep coma, but does not include systemic circulatory failure, e.g. shock, Stokes-Adams syndrome, or hypertensive encephalopathy.

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SECTION 6:

Procedures for Data Collection - Screening

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SECTION 6 - PROCEDURES FOR DATA COLLECTION: SCREENING

6.1 Smoking History

The smoking questionnaire is part of the general questionnaire and has been produced in final form by the Geneva Working Group of October 1981 (see protocol - WHO/MNC/82.1, page 25)).

It represents a compromise among different proposals and derives, at least practically, from the WHO Cardiovascular Survey Methods questionnaire. It can be self-administered if it is sent to the home of the invited persons together with the invitation to the examination; or it can be administered by a technician or nurse on the screening site.

The same procedure, however, should be applied throughout the study in the same centre.

In the case of self-administered procedures, the questionnaire should be reviewed by a technician or a nurse for completeness and consistency of answers.

In the case of direct administration some general rules should be followed:

- Use the same wording written on the questionnaire;
- Ask the questions a second time and in the same way if on the first occasion the subject does not answer or appears not to have understood;
- Ask the questions a third time using different wording but having the same meaning if the subject again does not answer or understand;
- Record answers and do not interpret them;
- Do not induce certain answers;
- Ask all questions and record all answers unless otherwise stated.

Interviewers should be trained and their performance evaluated and tested for precision and accuracy.

The protocol states that the smoking questionnaire should be validated, if at all possible, by physical methods such as carbon monoxide or plasma thiocyanate. If such measurements cannot be done on all subjects, do them on a subsample of one out of 10 subjects, irrespective of their smoking history. Standardization of such measurements cannot be proposed here but a description of the methods employed and the evaluation of laboratory precision (by repeating 10 to 20 measurements on a pool of sera at least once at each screening is required).

6.2 Blood Pressure Measurement

It is important that measurement of blood pressure (BP) is as precise as possible. This is essential for valid comparisons. Therefore a strict order of doing BP measurement should be kept as a fixed routine.

1. The subject should be instructed to avoid the following activities for at least one hour before the BP measurement: strenuous exercise, eating, drinking of anything other than water, smoking, drugs that affect the blood pressure; full bladder affects the blood pressure and patients should be advised accordingly.

2. The participant should have removed outer garments, jackets, etc. The sleeve of shirts, blouses, etc. should be rolled up so that the upper right arm is bare for the blood pressure cuff. The shirt should not constrict and the blood pressure cuff should not be over the garment. Garments must be removed if obstructing and a short-sleeved jacket provided.
3. The examination should take place in a quiet room with constant controlled temperature.
4. The equipment used should preferably be the random-zero sphygmomanometer. The cuff (bladder-size) should be 12-12.5 cm wide and sufficiently long to surround at least 2/3 of the upper arm.
5. The BP should be measured after resting with no change of position for at least 5 min., in sitting position and using the right arm - unless there is a deformity. When seated the subject's arm should be allowed to rest on a desk so that the antecubital fossa is level with the heart. To achieve this either the position of the subject in the chair should be adjusted, or the arm may be raised or lowered on a comfortable support. The subject must always feel comfortable.
6. The cuff should be applied firmly enough to prevent slipping. The rubber tubes should lie symmetrically on each side of the cubital fossa (to have the central part of the rubber bladder covering the brachial artery). The lower edge of the cuff should be 2-3 cm above the cubital fossa, to allow sufficient room for the ball of the stethoscope. The top edge of the cuff should not be restricted by clothing.
7. The observer should be in a comfortable position in relation to the examination table. The sphygmomanometer's mercury column should be in a perfectly upright position, the centre of it at the eye level of the examiner. The mercury column should face the observer and should not be in the subject's view.

The cuff should be connected now with the sphygmomanometer.

8. After the subject has rested 5 minutes in this position - during which the whole process of BP measurement could be explained to him/her - first the peak inflation level should be established. This is the level to which the pressure should be raised for the first blood pressure measurement.

The procedure is the following:

- a. Feel the subject's radial pulse with your left hand fingers;
 - b. Inflate the cuff and note the level of the top of the meniscus of the mercury column at the point when the radial pulse disappears. The immediately deflate the cuff by disconnecting the cuff and the sphygmomanometer.
 - c. Write down the level of the mercury column (where the radial pulse disappeared) to the nearest 2 mm reading and add to this number 30: this sum is called the peak inflation level.
9. Reconnect the cuff and the sphygmomanometer and wait for at least 30 seconds, or raise the arm for 5-6 seconds. This is to allow the return of venous blood to the forearm).

Locate the brachial pulse. The point of maximal pulsation, immediately below the cuff where the bell of the stethoscope should be placed. If it is not possible to feel the brachial pulse, the bell of the stethoscope should be placed over the area of the upper arm immediately inside the biceps muscle tendon. The bell should not touch the cuff, rubber or clothing.

Looking at the manometer with the centre of the scale at eye level, and the column perfectly upright, inflate the cuff rapidly to a pressure equal to the peak inflation level. From this point let the column of mercury fall at a rate of 2 mmHg per second.

Continue to reduce the pressure steadily at this rate until recording the systolic and phase 5 diastolic level. Then deflate the cuff rapidly (as above).

Blood pressure values should be recorded to the nearest 2 mmHg (reading from the top of the rounded meniscus. If the top of the meniscus falls half way between two markings, choose the marking immediately above.

10. Reconnect the cuff and the sphygmomanometer, raise the arm for about 5-6 seconds, or wait at least 30 seconds, and then repeat the measurement exactly the same way the first one was carried out.

Whenever having difficulties in hearing the sounds, the cuff must be completely deflated and at least 30 seconds must pass before making the next measurement.

11. Record the values of both measurements, then take the mean value, representing the subject's BP.

The above procedures for BP measurement should be applied regardless of the instrument used (i.e. simple mercury, random-zero or School of Hygiene sphygmomanometer).

For the random-zero machine additional instructions apply. These include:

- a. Connect the cuff tubing to the random zero device.
- b. Ensure that the mercury reservoir valve is in the operating position, i.e. turned fully to the right and extending past the right side of the case; turn the bellows cock on the face of the device to the right, to the position marked OPEN.
- c. Turn the thumb wheel at the right side of the device, by gently stroking it two times with the thumb of the right hand. If the wheel is not free to spin in either direction, the bellows are not completely deflated and the bellows check position should be rechecked.
- d. Inflate rapidly by the same method as for the standard device, to the peak inflation level for this series of random zero readings.
- e. By closing the bulb thumb valve, hold the pressure at this level for five seconds (count to five slowly), and then turn the control valve to the left, to the position marked CLOSE.

- f. By carefully controlling the thumb valve, with the bell of the stethoscope over the brachial artery deflate the cuff at 2 mm/second until the mercury level is 4-6 mm below the diastolic reading.
- g. Open the thumb valve fully and disconnect the tubing to the random zero device, allowing the mercury to fall to its zero level for this reading.
- h. Record the systolic and 5th phase diastolic readings, uncorrected.
- i. Read the zero level for this reading and record it on the form in the spaces provided beneath the uncorrected systolic and 5th phase diastolic readings. Subtract the zero level to obtain the correct readings and record on the form.

6.3 Serum Cholesterol (See report of Prague Lipid Workshop, Annex I of WHO/MNC/82.2).

6.4 Height and Weight

HEIGHT

Procedures

1. Height is measured in conjunction with the weight measurement. It may precede or follow this procedure.
2. The height rule must be taped vertically to a hard flat surface, with no moulding, with the base at the floor level. A carpenter's level should be used to assure vertical placement of the rule.
3. The floor surface must be hard (tile, cement, etc.) and cannot be carpeted or have other soft materials. If only a carpeted surface is available, a wood platform should be laid down to serve as the floor. A mat or small carpet should be used between the chair and rule.
4. The participant is asked to remove his/her shoes and heavy outer garments (jackets, coats, etc.).
5. To measure height, the participant should stand with his/her back to the height rule. The back of the head, back, buttocks, calves and heels should be touching the rule, feet together. The top of the external auditory meatus (ear canal) should be level with the inferior margin of the bony orbit (cheek bone). This position is aided by asking participant to hold head in a position where he can look straight at a spot, head high, on the opposite wall.
6. Place the triangle on the height rule and slide down to head so that the hair is pressed flat.
7. Record information on survey form to nearest centimetre. For example, if 187.4, record as 187; If 187.5, record as 188. If 187.6, record as 188.

8. Self-reported heights are not acceptable in ambulatory participants and should not be reported (mark as refusal). Only persons who are not ambulatory (e.g. amputees) may self-report their heights. Be sure to note this on the form.
9. To measure extreme heights, a short rule is used in addition. It is placed at the top of the long rule and the extra height is added.

BODY WEIGHT

Procedure

1. The floor surface on which the scale rests must be hard and cannot be carpeted or have other soft materials. A mat or small carpet with non-skid backing should be used between the chair and the scale.
2. The scale should be balanced with both weights at zero and the balance bar aligned.
3. The participant should have removed his/her shoes and heavy outer garments (jackets, coats, etc.).
4. The participants should stand in the centre of the platform as standing off centre may affect measurement.
5. The weights are moved until the beam balances (the arrows are aligned).
6. The weight is read and recorded on form. Record weights to the nearest 200 g.
7. Under no circumstances is the participant to self report his/her own weight or do the reading of the scales.
8. Self-reported weights are not acceptable in ambulatory persons. Refusals to be weighed should be recorded as refusals. Only participants who are not ambulatory (e.g. amputees) may self report their weights. Be sure to note this on the form.

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SECTION 7:

Quality Control of Data Gathering Procedures

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SECTION 7 - QUALITY CONTROL OF DATA GATHERING PROCEDURES

7.1 Introduction

Since the purpose of the Monica Project is to study relations between time trends in cardiovascular risk factors and diseases, it is of critical importance to maintain the data gathering procedures unchanged over time within study centres. Differences in methods in especially disease monitoring may arise between centres, but these are less critical. However, attempts should be made to standardize all data collection procedures as strictly as possible between centres as well. The most important thing is to collect the same primary data in the same way in all centres.

7.2 Quality Control

7.2.1 Screening techniques

A high response rate in screening surveys is extremely important, since non-respondents tend to have different behavioural and health characteristics from the rest of the sample, and their omission therefore results in bias. Since the likelihood of bias depends on the cause of non-response, each centre should report the numbers that fall into various categories, for example, removed since census, on holiday, ill, death, or refused to take part.

Successful recruitment requires careful preparation through personal contacts and an educational campaign so that individuals will be motivated to join the study and community leaders will have pride in their association with the project. It is particularly important to obtain the approval and recognition of the medical staff directly concerned with the care of the population under study. Study propaganda involves many techniques, including letters of endorsement by important persons, public lectures with illustrative films, and other groups and personal contacts designed to build interest, understanding and confidence in the study.

Though a 90% response rate may often be a reasonable goal, extra efforts should be envisaged to achieve recruitment among the 10-20% of non-respondents often encountered. If resources are insufficient, efforts may have to be concentrated on a random sample of the non-respondents.

The reproducibility of the screening methods can be tested in preliminary studies and at intervals throughout the main study. It is more difficult to determine the validity of the method, i.e. whether it measures what the investigator wishes it to measure. It is useful to plan a checking procedure and to collect data from other sources in order to assess to what degree the reported intake has been altered by the observer effect or other conditions of data collection. A related problem is the extent to which the behaviour or other items measured is usual or representative of the time period to which the data will be applied.

Training in blood pressure registration is necessary, since systematic differences between observers may be larger than the true differences under investigation between populations. Training films are available that demonstrate observer variation and allow calibration to an average for the group tested. Realistic playback of tape-recorded Korotkoff sounds through a

stethoscope earpiece is used first to train and then to test the observer, who activates stop watches at the start of a rundown and arrests them at systolic and diastolic endpoints. "Standard values" from readings of experienced observers are compared with the trainees' average for twelve patients, and the training continues until the systematic differences from the standard are at a minimum. As a calibration procedure the tape-recording can be used to check for trends - for example, between the start and close of a survey.

With or without tape or film material, training on actual subjects is required for the field staff. This is best done by assigning a group of two or twelve subjects to each of the several observers for replicate readings and analysis of the variations. It is essential that significant systematic variations should be eliminated between observers by repeated training. During the field study, a random allocation of a sample of the subjects is made for replicate readings by each observer to assess the quality of the pressure reporting and to detect systematic observer differences. When more than one examiner is involved, it is preferable that examiners should operate simultaneously, dealing with alternate subjects. Although any systematic observer differences would seriously affect the distributions, such a routine would largely preserve the validity of blood pressure relationships studied within the population.

The blood pressure values reported should be carefully described. The first recording made at examination is the one usually reported. Tabulations are made of both the fourth and the fifth phase diastolic levels. Total distributions by age and sex should be provided in the report. Examples of distributions of blood pressure readings by individual examiners should be given.

To maintain quality within study centres against the "off-days" and time-trends in reading, and to improve the level of comparability between centres, a systematic and permanent method of detecting, reducing and making allowance for observer variation is necessary.

In the absence of a calibration standard, laboratory quality control may be based in two independent readings of all records, disagreements being adjudicated with a third person. Residual disagreement between experienced readers in this scheme is extremely low, and reproducibility of the entire representing all major ECG categories, inserted into each batch of current records. If duplicate coding of all records is impracticable, it may be performed on an enriched sample. The procedure of arbitration allows continuing assessment of inter-observer variation on large numbers, detection of systematic differences and errors of "omission", etc.; it also permits a check on intra-observer variation and time trends in coding.

Observer variation is gradually lowered to an irreducible minimum within a centre, and attention is given to comparability between centres. This is improved by common training, by exchange of personnel and by tightening the quality control of individual centres.

Despite adequate precision in determination of serum lipids and other variables within a laboratory, important systematic differences may occur within and between laboratories.

Baseline values from samples obtained on two occasions a few days or weeks apart are recommended for improved characterization of the individual level, and seasonal and technical variation should be assessed within each study centre.

7.2.2 Monitoring of diseases

The reliability of the disease monitoring procedures consists of two components:

1. the coverage (completeness) of the case-finding procedures, and
2. accuracy in applying the given diagnostic criteria to identified cases.

It is of central importance to maintain both the coverage and diagnostic procedures unchanged within each study centre over time.

Repeatability tests of case validation should be arranged at regular intervals. They include reclassification of samples of hospital record abstracts and death certificates, as well as reabstractions of samples of hospital records. Both procedures should be carried using a blind design.

7.3 Internal quality control

To be prepared.

7.4 Training

In a longitudinal study such as the Monica Project, multiple observers over time or change in the manner a single observer interprets data threatens the stability of the observations. A set of clear and concise data collection forms is the most important intervention for insuring the collection of complete, stable and accurate data. The forms should be developed to reflect the criteria and a centre should budget enough time to create and test multiple drafts. One test of the adequacy of the forms is to have a "naive" observer interpret the forms using the printed guidelines. To the extent that they can do this with sufficient accuracy to satisfy the investigators, the forms are adequate. When developing questions, one particular problem that will arise is the use of adjectives and adverbs as modifiers; they usually only provide the illusion of concise definition. For example, in the question, "Was there a recent myocardial infarction?", "recent" implies different intervals to different people and will lead to inconsistent data recording. Therefore, it is suggested that either the modifier be dropped altogether to include all myocardial infarctions or an explicit interval, for example 28 days, be used in its place. A second problem is asking questions with multiple contingencies: for example, if the question "Did the patient receive cardioversion for ventricular fibrillation?" is asked, and the abstractor responds with "Don't know" or "Not recorded", it is not clear for analysis whether the patient was cardioverted but the reason was unknown and whether there was no record one way or the other about the cardioversion itself. To avoid this problem, the question should be divided into two separate questions; that is, "Did the patient receive cardioversion?", and if the answer is "Yes", then ask "Was the cardioversion for ventricular fibrillation?".

When preparing the guidelines for forms preparation, those data elements which become labelled "self-explanatory" should be examined closely. The "self-explanatory" items usually involve implicit assumptions of meaning and if the implicit assumptions are not made explicit, they create severe problems with reliability.

7.4.1 Hospital record abstracting

When training observers for the abstraction of hospital records it is more important to focus on the accurate completion of the forms rather than on the understanding of cardiovascular diseases in general. A set of test records should be developed which offers a broad range of examples and problems which will be encountered by the abstractor. These records can be used both to train the abstractor and for abstractor recertification every three to four months.

The goal of the quality control effort is to detect and eliminate bias and errors. Bias, for example, appears when an abstractor answers "no" rather than "not recorded" to the question "Was there a history of previous myocardial infarction?" even if no mention is made either way in the chart and the abstracting rules say that the chart must have an explicit statement about the presence or absence of a prior MI for the abstractor to answer "yes" or "no". Errors will appear in the demographic data, and because large numbers of such data are collected from each chart, only a few charts need to be reviewed to detect unacceptable error rates.

Approximately one of 30 to one of 50 records should be reabstracted by a second observer to check for bias and unacceptable error rates on the part of the abstractor.

7.4.2 Death certificate validation - interview of witnesses

The ideal interviewer for this job is one who has had experience in interviewing but is not a health professional. The health professional is avoided to prevent the preconceptions which they bring with them onto a job. Interviewer training should begin with a review of basic interviewing techniques and with tapes of interviews which demonstrate these skills. Elizabeth Kubler-Ross' book On Death and Dying may also be assigned to acquaint the interviewer with the grieving process and to help them feel comfortable with the fact that the interview will not cause unnecessary grief or emotional trauma to the respondent.

Role playing is also a helpful exercise. The trainee knows only the death certificate diagnosis and interviews the supervisor who has a scenario of the events surrounding the death of interest. If more than one interviewer is being trained, the other trainees can observe the session and participate in the discussion at the end of the interview.

It is also helpful to record the interviewers voice during actual interviews. These are then reviewed with the supervisor to detect leading questions or missed opportunities for follow-up of leads given by the subject. Although it only contains the voice of the interviewer, this tape will also help the interviewer reconstruct the interview from his or her notes.

Faulty interviewing technique can generally be divided into the use of leading questions and the failure to probe into indefinite answers. To avoid leading questions, the interviewer should be taught to use general rather than specific probes. For example, when trying to establish whether the decedent became short of breath before he died, rather than ask "Did your husband become short of breath before he died?", the interviewer can ask "Could you describe your husband's breathing for me?"

A lack of adequate probing, on the other hand, leads to the collection of uninterpretable data. An example of this would be when the interview subject makes a statement like "His breathing got real funny just before he died", and the interviewer fails to try to define "funny". In this case "funny" has no explicit meaning, so the interviewer should probe with the question "I'm not sure I understand exactly what you mean by "funny". Could you describe this for me?".

Reinterview can also be used as a quality control procedure. At the end of the interview, the interviewer simply asks permission for the project to call the respondent back if clarifications are needed. The respondent will probably approve, and a sample of respondents can be reinterviewed by the supervisor at a later date.

7.4.3 Blood pressure measurements

The determination of BP is one of the most frequently utilized procedures in medical practice, but unfortunately supported by the least formal systematic training.

If we accept the necessity of standardization of methods in epidemiology, we have to develop a standard BP-measuring technique with a standard equipment.

The training course should deal in detail with all the elements involved in BP measurement:

1. The principles of Korotkoff sounds and their sequence.
2. The equipment: (a) stethoscope (with bell); (b) sphygmomanometer (type) and its maintenance.
3. Observer: (a) hearing test? (b) digit preference.
4. The technique of measurement.
5. Sources of error: systematic; random.

Practical training

1. Tape recordings:

Among the existing training programmes the method developed by R.J. Prineas is recommended. (The timex could be replaced by 3 stop-watches).

Four cassettes at \$20 each (\$80 for the complete set) plus \$5 shipping, as well as a Blood Pressure Manual at \$8.50 plus \$2 shipping, are available from: Norman Burke, Vital Signs Institute, PO Box 981, Bensalem, Pennsylvania 19020.*

2. Training on subjects:

Measurement with double (Y-tube connected) stethoscopes with each observer operating the bulb alternately. Comparison should be made between observers (interobserver variation between supervisor and observer - systematic error - and between repeated measurements - intraobserver variation). The measurements should be recorded on training sheets and kept for further comparison.

* 1982 prices

7.4.4 Venipuncture and collecting, storing and shipping serum

To be prepared.

7.4.5 Data management and forms control

To be prepared.

7.4.6 Training for ECG coding technicians

As it is an unavoidable condition to code ECGs in a uniform bias-free way in order to obtain comparable data, ECG coders of the participating centres should get special training in this field. Training will be organized by the ECG Reference Laboratory, Budapest, Hungary. ECG classification and standardization procedures will be based on the Minnesota Code. Individual coders will be standardized rather than centres.

ECG standardization procedures:

To establish baseline differences in the interpretation of the Minnesota code between coders, training sets of ECGs will be prepared. In the first training set attention will be focussed on Q-QS items, T-wave abnormalities, ST elevation and depression as well as ventricular conduction abnormalities.

A second training set will be constructed on the basis of a screening programme, that is a series of normal and moderately abnormal ECGs will be collected.

Coding instructions will be given. Codes must be sent back to the Reference Laboratory. After receiving these data, the Reference Laboratory will send each coder the reference codes. Intra- and interobserver variation will be analysed statistically and will be presented in a tabulated format for easy reference. After the establishment of differences and misinterpretations in coding, the attention of each coder will be drawn to his/her weak points. Suggestions for improved performance will be provided.

Regarding the common mistakes in coding, short special training courses for coders will be organized to improve their knowledge and to code ECGs in a more uniform way. The curriculum of the course will be elaborated on the concrete experiences deriving from the training sets. Lectures, demonstrations will be held to promote standardization in measurement.

Special ECG series will be collected for collective coding in order to evaluate them in a more uniform way and to discuss concrete problems on coding. The new Minnesota classification system for ECG pattern change will be demonstrated.

After giving training programmes, first checking ECG set will be sent to the centres. Data will be analyzed by the above method. Coders who achieve equal or better results than the limit determined can get certification (see Section 7).

The Reference Laboratory will provide consultant advice for centres which can not get certification to give further advice on coding and to help coding procedures.

A second checking ECG set will be sent to the unsuccessful coders in order to get certification.

After having certification stability of quality performance in coding will be checked yearly by sending ECG sets for coding. Not only Xerox but the original ECG copies will be circulated among the centres to avoid misinterpretation deriving from technical problems.

The Budapest Reference Laboratory is willing to keep in permanent contact with the Minnesota Reference Centre in order to compare their codes and to help with any new methods of standardized ECG evaluation.

7.5 Certification and recertification

7.5.1 Blood pressure technicians

The method of measuring blood pressure can be learned quickly and it is far from being a "doctor's job" only. Paramedical personnel can perform it sometimes more precisely, as they are free from "intuition". But whoever takes up the task of measuring BP, they must be trained and tested before being certified for the job.

In screening programmes, when more observers make measurements, they have to be as alike as possible. For example, all of them paramedical technicians and in addition all women. (Consider the possibilities that the reaction of the subject is likely to be different towards a nurse than towards a doctor; or that women observers obtain different BP-measurement in men, than men doing the same task).

The aim of a training and retraining programme is to develop maximum precision and standard recording. This is necessary to avoid random and systematic error. Random error will occur if an observer occasionally neglects the controllable factors during BP-measurement. Systematic error will arise from an action which consistently results in a higher or lower BP-reading. Examples: severe hearing loss for low frequency sounds, digit preference, prejudice, i.e. "expecting a BP", consistently using another technique (left arm, lying position, etc.). Therefore continuous attention should be paid to BP-measuring techniques and training. During the practical training means of measurements are used for comparison between observers and supervisor.

If the mean value or range of an observer's measurements differs markedly from the fellow observers, further training is necessary. Retraining and retesting of observers should be carried out at regular intervals in order to maintain the validity of BP measurement.

Any observer, continually making blood pressure measurements should be retested at 6 monthly intervals. Observers whose mean value of measurements differs from the other observers should be retested sooner. Observers with consistent systematic errors cannot be qualified for taking BP-measurements.

7.5.2 Certification and recertification in ECG coding

After carrying out training procedures (see Section 7), the first checking ECG set will be sent to each coder. A certificate is obtained if agreement between individual and reference codes is equal to or more than 90%.

Coders who fail in the first certification possibility have to repeat the training procedure. A second opportunity will be given to get a certificate. Coders who cannot solve a second checking ECG set at a 90% level should be refused.

Certificates must be renewed yearly. In order to qualify, the Reference Laboratory will send out checking ECG sets to the coders each year. For renewing coding certificates at least 90% agreement should be reached again.

7.6 Equipment maintenance

7.6.1 Sphygmomanometers

1. The mercury sphygmomanometer should be checked regularly, at least every 6 months.
 - Check the level of mercury: The top of the meniscus of the column should be in line with the zero mark in the manometer. If the mercury level is too high or too low it should be corrected by subtracting or adding mercury to the reservoir. You can check the manometer case by looking for mercury globules which indicate mercury loss. In the case of mercury leakage, return the sphygmomanometer to the service centre immediately.
 - The manometer tube should be checked for dirt, which is often oxidized mercury. By removing the screw at the top of the manometer, you can clean the tube with pipe cleaners.
 - The cuff and the pressure of the cuff should be checked also. The adhesive parts of the fabric cover and the cover itself should be checked. When the inflated cuff is wrapped around a column - similar to an arm - and the valve of the bulb is kept closed then the mercury column should remain steady or fall at a rate less than 1 mm each second. If the mercury falls more quickly, then all rubber tubing connections, the rubber bladder, the bulb and valves should be checked or replaced.
 - The bulb should be checked for leakage, which can be often heard as a hissing sound from the bulb itself. If the valve is difficult to turn, silicone oil may be applied, but if this manoeuvre fails the bulb should be discarded.
2. The Random zero and London School of Hygiene sphygmomanometer should be checked with the same regularity and method as the mercury sphygmomanometer. For additional recommendations look at the instructions given for these instruments.

7.6.2 Weight scales

To be prepared.

7.6.3 Laboratory equipment

To be prepared.

7.7 Quality Control Reports

To be prepared.

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SECTION 8:
Data Management and Analysis

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SECTION 9:
Coordinating Centre

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ANNEX I

Standardization of Lipid Measurements

See document circulated separately.

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ANNEX II

Monica investigators and committee membership

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ANNEX III

Criteria for entry into main study after "test" period

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ANNEX IV

Distribution list for each centre

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ANNEX V

Updating Procedures

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ANNEX V: UPDATING PROCEDURES

Procedures for updating procedures

Procedures laid down by the Manual of Operations and the Operating Protocol should be rigidly adhered to for the collaborative project. If a centre wishes to follow a particular procedure of its own which is different it will need to employ both the standard and the local procedure (e.g. in classification of events) to ensure comparability with the core study.

It is hoped that any difficulties, ambiguities or contradictions in the documentation will be discovered and corrected in the pilot study period and the documents will be revised for the main study. However, any centre discovering or experiencing particular problems should notify the coordinating centre. If a simple answer is not forthcoming the coordinating centre will send a circular to all principal investigators for comments and suggestions, to find out the size of the problem and any possible remedies. The results will be sent to members of the steering committee and the problem dealt with by post or at the next committee meeting.

The following problems could arise:

1. Centres following different procedures without realizing it. The coordinating centre should seek to minimize this by central quality control, circulation of sample histories, etc. If it occurs some centres may need to recode their cases.
2. Centres wishing to change procedures. A two thirds majority of principal investigators would be needed to effect this and new and old procedures would have to be run in parallel for a prolonged period to assess the systematic bias the change might create.

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APPENDIX I

Finnish manual

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APPENDIX II

University of Minnesota
Laboratory of Physiological Hygiene Survey Manual

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APPENDIX III

University of Minnesota
Project Manual

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