Background, Development and Organization of MONICA

#1 Background to the WHO MONICA Project

The post-war epidemic

Peace and prosperity and the control of infections through antibiotics and vaccination all promised longer life expectancy after the Second World War. However, this promise was not fulfilled in many countries, particularly in men. A new form of heart disease, going under different names—degenerative, atherosclerotic, ischaemic, or coronary heart disease—but basically one condition, was rapidly increasing. The most economically advanced and industrialized countries seemed at greatest risk. Large increases in such mortality had begun in many different countries, some as early as the 1920s, but in others only a decade or two later. These countries, led by the United States of America, initiated studies to identify the causes of this disease, previously labelled as degenerative and, by implication, a manifestation, and therefore inevitable consequence, of increasing age.

Framingham

The Framingham Study, the best-known study, and a model for many others, was launched in the early 1950s (1). Several thousand men and women in Framingham, Massachusetts, were examined for certain personal factors, suspected, and subsequently shown through many years of follow-up, to be powerful and consistent indicators of increased risk of coronary heart disease. The concept of risk factors was born. The most consistent and powerful of these in explaining coronary risk, the classic risk factors, were cigarette smoking, blood pressure and blood (serum or plasma, also known as total) cholesterol. Others were less common (diabetes mellitus), less consistent (obesity and exercise) or less readily measured (diet, alcohol and psychosocial factors).

Seven Countries

Soon after the initiation of the Framingham Study came an international collaboration led from Minneapolis in the United States, the Seven Countries Study (2). It sought to explain the large variation in death rates from coronary heart disease in different countries. Study populations, some occupational, some residential, in seven countries extended over the full range of mortality rates, from Finland (high) to the United States of America, the Netherlands, Italy, Yugoslavia, and Greece to Japan (low). This study found the classic Framingham risk factors to be of differing importance in determining variation in coronary risk between whole populations in different countries. Obesity and physical exercise accounted for little, as did cigarette smoking. Blood pressure was of some significance, but the dominant role went to cholesterol. The average blood cholesterol concentration varied significantly across populations. It correlated with the amount and type of fat in the diet and correlated strongly with population coronary disease rates.
**Cardiovascular Survey Methods and ten-day seminars**

For cross-population comparability, studies in cardiovascular epidemiology needed standardized methods of ascertainment and people who knew how to use them. By the 1960s the former were sufficiently developed for the World Health Organization to publish a manual prepared by Henry Blackburn from Minneapolis and the *Seven Countries Study* and Geoffrey Rose from the London School of Hygiene and the British Whitehall Study (3), the now classic *Cardiovascular Survey Methods* (4). Through the Research Committee and the Council on Epidemiology of what was then the International Society and Federation of Cardiology, an international faculty of teachers initiated annual ten-day teaching seminars. The first took place in Makarska in Yugoslavia in 1968 (5). They continue to this day. They introduced the concepts of cardiovascular epidemiology and of conducting field surveys to likely candidates, often trainees in cardiology. The seminars produced a cadre of young initiates, and a network of contacts for international collaboration.

**Coronary care and the European Myocardial Infarction Registers**

During the 1950s and early 1960s ambulatory treatment of angina pectoris, the chronic symptom of coronary heart disease, consisted of pain relief with a limited range of nitrate drugs. For myocardial infarction (coronary thrombosis), an acute medical emergency, treatment was morphine, anticoagulants and extended bed-rest. Management was then revolutionized by the electronic monitoring of patients with myocardial infarction in coronary care units (6), with potential resuscitation from cardiac arrest by electric defibrillation and mouth-to-mouth respiration. New drugs were being introduced. Claims that cardiac mortality was being halved in such units fitted strangely with rising population mortality rates. This led to an initiative by the European Regional Office of the World Health Organization in the late 1960s to establish *Myocardial Infarction Community Registers* (7) in which the incidence and outcome of acute coronary events would be studied on a whole-population basis. Both hospital-ized myocardial infarction, and out of hospital coronary deaths would be studied together to assess the known and potential impact of coronary care. The registers established standardized techniques for heart attack registration not previously incorporated in *Cardiovascular Survey Methods*. They also confirmed that the great majority of coronary deaths were occurring in the community, outside hospital, and largely inaccessible to hospital-based acute coronary care.

**The American decline and the Bethesda Conference**

Concealed from immediate recognition by the instability of intermittent winter influenza epidemics, mortality rates from coronary heart disease in the United States of America began to decline in the early 1960s. Similar trends appeared in other New World countries such as Australia and Canada, while coronary disease mortality was still rising or stable elsewhere. The decline in mortality in the United States caused considerable excitement. It was analysed at a seminal conference organized by the US National Heart Lung and Blood Institute at Bethesda in Maryland, USA in 1978 (8). At this conference Piša, of the World Health Organization in Geneva, with Epstein (later also important in MONICA) showed comparative data on trends in cardiovascular mortality after the Second World War for a number of different countries (8), work that Piša later extended with Uemura (9). The Bethesda conference demonstrated that the American decline was probably genuine, but inadequately explained. Despite thirty years of cardiovascular research, information on risk factors, morbidity and mortality was incompletely integrated. There had been variation and inconsistency in the definitions and
populations studied. What was needed was long-term monitoring of mortality, morbidity and risk factors in the same defined populations experiencing different trends in mortality, to establish the underlying patterns and associations. This was the background to the WHO MONICA Project, first proposed after the Bethesda conference in 1979, and undertaken across four continents in the 1980s and 1990s, in parallel with similar studies that took place in the United States of America (10–13).

References

Hugh Tunstall-Pedoe

#2 MONICA Hypotheses and Study Design

Introduction
The following aims, objectives and hypotheses of the MONICA Project are taken from the original protocol of the early 1980s. The protocol has undergone subsequent minor revisions. Numbered notes and commentary are provided as explanations for the current reader.

Name
Multinational Monitoring of Trends and Determinants in Cardiovascular Disease. Hence the MONICA Project (1).

Objectives
To measure the trends in cardiovascular mortality and coronary heart disease and stroke 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 socioeconomic features measured at the same time in defined communities in different countries (2).
Hypotheses
Changes in cardiovascular mortality might be related to a change in disease incidence (3), or a change in case fatality, or both. A change in incidence could be related to change in any of the known factors such as cigarette smoking, blood pressure, blood cholesterol, diet, weight and exercise (4), or other unrecorded factors. A change in case fatality could be related to changes in medical care, or in the natural history of the disease.

The MONICA study will involve measurement of:

- incidence rates (3)
- case fatality
- risk-factor levels (4)
- medical care (5).

These can be used to test six possible associations:

- risk factors versus incidence
- medical care versus case fatality
- incidence versus case fatality
- medical care versus incidence
- risk factors versus case fatality
- medical care versus risk factors.

Although the six associations can be tested within the MONICA Project for both coronary heart disease and stroke, a small number of main null hypotheses have been formulated:

Main (coronary) null hypothesis
For the population Reporting Units there is no relationship between:

- 10-year trends in the major CVD risk factors of serum cholesterol, blood pressure and cigarette consumption, (4) and
- 10-year trends in incidence rates (fatal plus non-fatal attack rates) (3) of coronary heart disease.

Second main (coronary) null hypothesis
For the population Reporting Units there is no relationship between:

- 10-year trends in case fatality rate (percentage of attacks that are fatal within 28 days), and
- 10-year trends in acute coronary care (5).

(Stroke hypotheses)
An analogous first hypothesis was subsequently formulated for stroke (replacing coronary heart disease with stroke, but otherwise identical), whereas a second main null hypothesis related trends in stroke and coronary-event rates (6). (For the population Reporting Units there is no difference in 10-year trends in event rates between stroke and coronary events.)

Contemporary notes for this Monograph
1. The name MONICA was an abbreviation of ‘monitoring cardiovascular disease’. It was suggested by Dr Tom Strasser who attended one of the early planning meetings in Geneva as a member of the WHO staff.
2. The ambitious sweeping objective owed much to the original MONICA Chairman, Dr Fred Epstein. It was followed in the protocol by a caution from the Rapporteur. ‘Collaborating Centres may wish to cover all these areas, but the basic protocol covers key items only, leaving the rest as local options’. There were components of the objective for which there were
then (and arguably still are) no standard cross-cultural methods of measurement.

3. The term ‘incidence’ is used loosely in ordinary medical parlance whereas in epidemiology it means the rate at which disease occurs in those previously free of the disease. In registering coronary heart disease it could be defined in several different ways. It was not possible in many MONICA populations to distinguish new from recurrent coronary events especially where these occurred as sudden deaths outside hospital. Likewise we only had information on the total population denominator, not how much of it was disease-free. MONICA in reality therefore used attack rates for incidence—that is the event rate for new and recurrent attacks combined. Angina pectoris was not included in incidence, which was confined to the major acute coronary events of myocardial infarction and coronary death. First event rates were calculated for those populations where reasonable data were available, but the denominator was the whole population, including those surviving previous non-fatal events.

4. In retrospect it is interesting to note the minor inconsistencies in the development of the protocol. It was revised a number of times. This applies to the key risk factors. When challenged by Dr Jeremiah Stamler at one of the early meetings in Geneva, to formulate null hypotheses in advance, we specified cigarette smoking, blood pressure and cholesterol, leaving out obesity, exercise and diet which had been mentioned previously. Obesity was subsequently brought back in the risk-factor score that was eventually used, although it made a very minor contribution, particularly in women, because of the small size of the coefficients that it attracted. Blood pressure became the systolic blood pressure. (See #35 Risk-Factor Scores.)

5. The hypotheses were formulated before MONICA had a clear statement of how and when medical care was to be recorded. This explains inconsistent use of the terms ‘medical care’, and ‘acute coronary care’ and ‘medical care in the attack’ used in different documents. Information on coronary care was recorded in relation to coronary events, including medication before the onset and at hospital discharge. This was specified by good fortune, as the impending importance of secondary prevention of recurrent attacks was not fully appreciated at the time. It was decided to record administrative information on medical care as a separate data item fairly late in MONICA. Although collected retrospectively, it was not incorporated into the hypothesis-testing analyses. (See #18 Health Services.)

6. Stroke hypotheses were formulated considerably later than those for coronary events. Stroke care was not a core data item. The status of stroke registration itself was officially ‘core’ but in practice ‘optional’. This was because centres could not be excluded from MONICA for refusing to study stroke, but centres that could do it needed to be able to inform their funding bodies that stroke was a core element of the study. It was recognized that without extending the age-range above 65, numbers of strokes being registered would make it unlikely that trends could be estimated with confidence, unless they were large.

**Study design**

The basic design of the MONICA Project first involved the designation of defined populations. Within each population, certain annual routine administrative data were required. These included demographic information on numbers by age and sex and official or routine data on numbers of deaths from different causes. MONICA investigators were then responsible for undertaking
registration of all coronary events within defined age groups (25–64) in both sexes over a period of ten years. Population risk-factor surveys were to be conducted at least at the beginning and the end of this period, and optionally in the middle. Coronary care was also to be monitored at least at the beginning and at the end, so that both of these data components were discontinuous. Centres were strongly encouraged to register strokes in the same populations at the same time as the acute coronary events.

Reference
MONICA Web Publications are also accessible on the Monograph CD-ROM

Hugh Tunstall-Pedoe

#3 Organization Chart of the WHO MONICA Project

The policy-making and management structure of the WHO MONICA Project is made up of the following components:

- Council of Principal Investigators—CPI (see #4)
- Principal Investigators—PIs
- MONICA Steering Committee—MSC (see #5)
- MONICA Management Centre—MMC (see #6)
- MONICA Data Centre—MDC (see #7)
- MONICA Quality Control Centres—MQCs (see #8)
- MONICA Collaborating Centres—MCCs (see #50–#84)
- MONICA Reference Centres—MRCs (see #9 and #43–#49)

Hugh Tunstall-Pedoe

WHO MONICA PROJECT: Organizational Chart

COUNCIL OF PRINCIPAL INVESTIGATORS

MONICA MANAGEMENT CENTRE
Cardiovascular Diseases Programme, WHO, Geneva

MONICA STEERING COMMITTEE

MONICA DATA CENTRE
National Public Health Institute, Helsinki

QUALITY CONTROL CENTRES(a)

MONICA COLLABORATING CENTRES

REFERENCE CENTRES OF OPTIONAL STUDIES(b)

a) Quality Control Centres:
   - Lipids (Prague)
   - ECG (Budapest)
   - Event Registration (Dundee)
   - Health Services (Perth)

b) Reference Centres:
   - Psychosocial (WHO, Copenhagen)
   - Nutrition (Bilthoven)
   - Vitamins (Bern)
   - Physical activity (Atlanta)
   - Drugs (Bremen)
   - Haemostatic factors (Belfast)
#4 Council of Principal Investigators (CPI) and MONICA Congresses and Symposia

Early meetings

Five preliminary meetings, involving a total of 61 different people were held between 1979 and 1981 to initiate what became the WHO MONICA Project. These meetings were held 17–19 September and 17–19 December 1979 in Geneva, 27–28 June 1980 in Paris, 13–14 April and 12–15 October 1981 in Geneva. (See #1 Background to the WHO MONICA Project and #15 Reminiscences of MONICA’s Rapporteur.) These meetings led to the publication and distribution in October 1982 of the document *Proposal for the Multinational Monitoring of Trends and Determinants in Cardiovascular Disease and Protocol* (1).

First numbered CPI: CPI-1

This (1) was the working document for the first numbered Council of Principal Investigators meeting (CPI) that took place in Geneva from 30 November to 3 December 1982. It was this meeting which began to give MONICA its structure for the next two decades by setting up the MONICA Steering Committee and initiating MONICA Memos and work on the *Manual of Operations* (2). This and subsequent Councils of Principal Investigators (CPI) were the MONICA Parliament, the highest policy and decision-making body of the WHO MONICA Project. They were composed of the designated Principal Investigators (PIs), who were the responsible scientific officer(s) of each MONICA Collaborating Centre (MCC), and MONICA country coordinators, if any; ex-officio staff including heads of the MONICA Management Centre (MMC), MONICA Data Centre (MDC), MONICA Quality Control Centres (MQCs) and MONICA Reference Centres (MRCs), Principal Investigators from Associate MONICA Centres, team members from MONICA Centres; consultants and support staff. For the full constitution see the MONICA Manual (3).

Later CPI Meetings

These were large and expensive meetings (see photograph). After the second meeting they moved away from Geneva and were hosted, organized and partially funded by individual MONICA Collaborating Centres (see list). Nine were held altogether. The Council had the key role to review, decide and plan the execution of the MONICA Project; to monitor and evaluate its performance; to define its scientific direction and to set its priorities and programmes. The Council reviewed and approved or rejected the MONICA Steering Committee’s proposals; it also elected new members of the Steering Committee and made structural changes to the MONICA organization. The Council acted as the highest policy and decision-making body of the MONICA Project and was guided by the principles of simplicity, cost-effectiveness, scientific rigour and importance and appropriateness of the research. The Council had to make timely decisions and monitor progress, respond to the needs of national MONICA programmes and have an active role in ensuring that MONICA maintained the highest scientific standards.

*Council of Principal Investigators was MONICA’s parliament*
*frequency of meetings limited by the cost*
*quality control, administration*
*networking on problems and optional studies*
*election of new members of MONICA Steering Committee*
*scientific congresses and symposia were separate*
progress; to exchange experience and information among PIs and team members; to review and to change the recommendations made by the MSC; and to elect the new members of the MSC. The emphases changed over time. Early meetings were concerned with interpretation and changes to the Protocol and Manual, quality control issues, coding workshops, optional studies; later meetings were concerned with publications. The MONICA Data Centre staff and Steering Committee took the opportunity to meet with Principal Investigators who had questions or problems.

**CPI-9**

The final CPI was held in Milan in 1998. Its main objectives were to ensure MONICA’s completion, decide future governance, revise publication rules, review progress with main hypotheses and decide on future MONICA collaborations. New publication rules, new authorship and citation rules were decided. These helped to speed up MONICA publication and to recognize contributions from authors. The composition of the MSC was also changed to include key advisers for finalizing the Project. The final structure of the MONICA Archive was revised and approved. The PIs also agreed upon the composition of the working groups appointed to prepare the final papers on the two main hypotheses of the Project. The CPI-9 also established the rules for voting and the quorum for changing the management and publication rules as well as the procedure for appointing future new members of the MSC by postal ballot. Last but not least, the CPI-9 approved the original outline of this MONICA Monograph and asked for it to be completed using the available funds.

**MONICA Congresses and Symposia**

The CPI meetings themselves were used as an opportunity to display posters from different centres. Three specific MONICA Congresses were also held, hosted by individual MONICA Collaborating Centres but numerous MONICA satellite meetings or sessions were also held within bigger international meetings in epidemiology, heart disease and stroke. The second and third MONICA Congresses were recorded in supplements to scientific journals (4, 5) and MONICA was responsible for, or a major contributor to, two other journal supplements (6, 7). The first was from a meeting organized by the National Institutes of Health in Washington. The most recent was from an International Epidemiological Association satellite meeting, at which major MONICA findings were presented (see table).

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<thead>
<tr>
<th>Meeting Place Dates Hosts Institution</th>
<th>Meeting Place Dates Hosts Institution</th>
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<tbody>
<tr>
<td>Udine, Italy 30/4–2/5/1990 F. Gutzwiller MONICA Switzerland</td>
<td>Udine, Italy 30/4–2/5/1990 F. Gutzwiller MONICA Switzerland</td>
</tr>
<tr>
<td>Helsinki 15–19/8/1987 J. Tuomilehto IEA satellite meeting</td>
<td>Nice 15–16/9/1989 French investigators and A. Bingham MONICA France</td>
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<tr>
<td>中关村, the oldest MONICA investigator</td>
<td>Yingkai Wu (Beijing), the oldest MONICA investigator</td>
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#5 MONICA Steering Committee (MSC)

**Early history (from SF)**

As it was originally envisioned, what later became the MONICA Project was to include about a dozen centres. As the Project developed in the early 1980s, interest was widespread and included most of the countries in Europe (then still politically polarized into East and West) and many in Asia, the western Pacific, and the Americas. This demanded a larger administrative structure than had originally been foreseen.

The first meeting of what became the Council of Principal Investigators was held in Geneva from 30 November to 3 December 1982. One significant impediment to progress was the lack of a data analysis centre to coordinate such items as data format, transmission, quality control checks, and the like. The Principal Investigators decided to establish a ‘steering committee’ to form a ‘ghost data centre’ to work on these issues. The MONICA Steering Committee (MSC) was therefore created at the meeting; membership included representatives from WHO Headquarters (Zbyňek Písa, Martti Karvonen) and the WHO European Office, (Vadim Zaitsev); the Data Centre Chief (then vacant); Hugh Tunstall-Pedoe as Rapporteur; and three elected Principal Investigators (Pekka Puska, Stephen Fortmann and Alessandro Menotti).

The first meeting of the MSC was held two months later, from 9 to 10 February 1983, in Helsinki, Finland. Pekka Puska, from the host country, was elected Chair for this session. The meeting focused on quality control, completion of the protocol, and the structure of MONICA. By then negotiations between WHO and the Finnish government to establish the Data Centre (MDC) in Helsinki were at an advanced stage. It was anticipated that Jaakko Tuomilehto would become Chief of the MDC.

The second meeting of the MSC was held in Liège, Belgium from 8 to 9 September 1983, in conjunction with the Annual Meeting of the European Society of Cardiology. Since there was no local host, chairmanship of the MSC was rotated to another elected Principal Investigator, Stephen Fortmann. This meeting also focused on the urgent needs of settling the protocol and manual of operations, the criteria for centres to be admitted to the study, and the organization and governance of the study. The MDC had still not been formally established, because of financial issues, but Jaakko Tuomilehto attended as MDC Chief-designate.

The other main organizational challenge was the establishment of a coordinating centre. Several sites had been interested in serving this role, but WHO could not find the financial support. The Cardiovascular Diseases (CVD) Unit...
at WHO Headquarters in Geneva thus became the *de facto* coordinating centre, and remained so throughout the study.

The third MSC meeting in Geneva, 11–12 January 1984, was followed by the second meeting of the Principal Investigators, also in Geneva, 28 February–1 March 1984. Stephen Fortmann was asked to continue to chair the MSC to provide continuity during this challenging period when the Project was getting organized but funding was insufficient. At the PI meeting Pekka Puska asked to leave the MSC and Stefan Rywik was elected to replace him. (Alessandro Menotti also later resigned owing to pressure of other work.) This established the tradition, later codified, of electing one new member of the MSC (and also a reserve member) at each meeting of the PIs. Another change occurred at this time, with Zbyněk Piša retiring as Chief of the CVD Unit and being replaced by Silas Dodu.

Stephen Fortmann remained Chair of the MSC until the third PI Meeting in Porvoo, Finland, 29–31 August 1985. From then on, chairmanship of the MSC went by custom, but also by formal election within the MSC, to the most senior of the elected PIs and lasted until the next meeting of the PIs, when this person would leave the MSC and a replacement would be elected. Financial constraints continued to plague the study, so meetings of the PIs, which should have been held annually, took place at 18-month intervals. Service on the MSC therefore lasted four to five years and chairmanship about one and a half years.

**Later history (from HTP)**

The MONICA Steering Committee continued to meet in Geneva between meetings of Principal Investigators and also met immediately before, during and immediately after the PI meetings. It was an exhausting schedule for those involved. In 1987 MONICA adopted electronic mail. Electronic mail, along with FAX machines, telephone conferences, and the Internet later revolutionized the way in which MONICA and the MONICA Steering Committee conducted business (see #11 *Communications in MONICA*). By early 2002 the MONICA Steering Committee had met 29 times in formal sessions but had also conducted 102 telephone conferences.

The core MONICA personnel on the MONICA Steering Committee were strengthened by the appointment of consultants (see #6 *MONICA Management Centre (MMC)*) and, in Geneva, by staff members from the Cardiovascular Diseases Unit, who attended the meetings, as well as by staff from the MONICA Data Centre. Support for these meetings was provided by Mary-Jane Watson who provided valuable continuity and tireless devotion over two decades. Although it sometimes had a large number of members, the MONICA Steering Committee benefited from a useful mix of fixed and changing members.

Chairmanship of the MSC was a demanding commitment. While most Chairs were pleased to give it up after eighteen months or so, this nonetheless marked the end of their involvement with the MSC unless they were re-elected. Several of them remarked on how strange it felt, after five years of work, to be no longer involved in telephone conferences or deluged with MSC e-mail. The Editorial Advisory Group of this Monograph has been one way of re-involving ex-Chairs with the current MONICA Steering Committee.

In addition to dealing with internal MONICA business, the MSC also tried to use its visits to Geneva to impress on WHO officials the importance of continued funding for the project. Cardiovascular disease was erroneously considered by many in the 1980s and early 1990s to be a problem only of the developed world (see #14 *MONICA and the Prevention of Cardiovascular Disease*). This misguided notion was unfortunately reinforced by the lack of MONICA centres in the developing world (see #10 *Recruitment of Populations* for the explanation). WHO was itself in the throes of severe financial difficulties over the MONICA decade that spanned from the middle of the 1980s to the middle of
the 1990s. Annual dues were missing from prominent defaulters, and there were wild fluctuations in the value of currencies. The MSC achieved less than it hoped in this respect. However, a fund was established in Geneva with donations from commercial sources which helped to support MONICA manuscript groups, data analyses and publications. What support there was from Geneva proved to be crucial in the longer-term.

Formal constitution and workings of the MONICA Steering Committee are described in the MONICA Manual (1).

Key personnel
Current (December 2002): Kjell Asplund (Chair), Philippe Amouyel (Publications Coordinator), Andrzej Pająk, Alun Evans, Hugh Tunstall-Pedoe (Rapporteur), Shanthi Mendis (MONICA Management Centre), Kari Kuulasmaa (MONICA Data Centre), Aushra Shatchkute (WHO, Copenhagen), Annette Dobson (statistical consultant).


Former consultants: Martti Karvonen, Ron Prineas, Manning Feinleib, Fred Epstein, Zbyněk Piša, Dale Williams.

In attendance: Mary-Jane Watson.

Reference
Diseases were staffed predominantly by medical officers from the socialist republics. Although medical officers changed over time, continuity was provided for almost the whole of the MONICA Project by the then Administrative Assistant, Mary-Jane Watson, a point of contact for very many MONICA investigators, although increasingly involved in other things later on. Secretarial continuity was provided by Margaret Hill.

Initially the Management Centre was responsible for almost everything, funding meetings of the Principal Investigators in Geneva, organizing MONICA Steering Committee meetings and partially funding the MONICA Data Centre. This latter role subsequently diminished as the Data Centre acquired its own funding. While MONICA had secretarial support in Geneva, it never had a full-time administrator or medical officer. Over the years, extraneous sources of funding financed the Data Centre and meetings of the Council of Principal Investigators, and data issues began to predominate. The role of the Management Centre, which was limited by its finances, centred on servicing the MONICA Steering Committee (which met increasingly infrequently), its regular telephone conferences, and in organizing the distribution of MONICA Memos (see #88 MONICA Memos).

The MONICA Management Centre initially had a stimulating role to play in the recruitment of candidate MONICA Collaborating Centres. Later it had the converse unenviable role of dealing with the fallout when some MCCs were failing. While some withdrew gracefully, others refused to walk off when shown the red card by the MONICA Steering Committee, and attempted to bring pressure through national representatives.

At its initiation the WHO MONICA Project was a joint project of the World Health Organization Headquarters in Geneva, and the European Regional Office in Copenhagen (EURO). Although this did not continue, the chronic diseases officer in EURO subsequently remained as a long-term member of the MONICA Steering Committee and coordinated an optional study (see #46 MONICA Optional Psychosocial Substudy (MOPSY)).

One of the key roles of the MONICA Management Centre was the recruitment and appointment of consultants to the project. These participated in the meetings of Principal Investigators, and later in the MONICA Steering Committee and worked on the project between these meetings.

Apart from future Principal Investigators, leading figures in the early days of the creation of MONICA, brought together by the Management Centre, were Zbyněk Piša (Czechoslovakia, now Czech Republic, Chief CVD Unit), his successor Silas Dodu (Ghana, Chief CVD Unit), George Lamm (Hungary, European Office), Tom Strasser (Yugoslavia, Medical Officer, CVD Unit), Martti Karvonen (Finland, consultant), Ron Prineas (USA, consultant), Manning Feinleib (USA, consultant), Fred Epstein (Switzerland, consultant), and later Dale Williams (USA, consultant). After MONICA was established, continuity in Geneva was maintained by Siegfried Böthig (GDR, now Germany, Chief CVD), Ivan Gyarfas (Hungary, Chief CVD) and Ingrid Martin (GDR, now Germany, Responsible Officer CVD). What was originally the Cardiovascular Diseases Unit in Geneva underwent reorganization and changes of building over the MONICA years. The present officer for Cardiovascular Diseases, in its reorganized structure, is Shanthi Mendis (Sri Lanka, Responsible Officer CVD).

The formal functions of the MONICA Management Centre are laid down in the MONICA Manual (1).

Key personnel


Administrative Assistant: Mary-Jane Watson. Secretarial: Margaret Hill.
Background and tasks

It was clear from the outset of the study, that each MONICA Collaborating Centre (MCC) would be responsible for the collection, management and analysis of its own data for local purposes. It was also accepted that a central facility would be needed to collect data from the MCCs to analyse them in testing the main hypotheses. The role of and requirements for such a facility, later known as the MONICA Data Centre (MDC), were defined in 1982 by a group of external consultants as the following:

- to function as the central repository and manager of core data received from the MCCs, (see #36 Data Transfer, Checking and Management)
- to undertake quality control of data
- to undertake interim and final statistical analyses
- to provide data sets to investigators carrying out other studies approved by the Steering Committee
- to consult with MCCs on data collection, data management, data processing and statistical analysis.

In addition to these functions, the MDC was closely involved in:

- preparation of data collection methods and instruments
- archiving of the Project’s data
- management of the Project in close collaboration with the Steering Committee and the Management Centre.

The MDC was not involved in management or analysis of data from the Optional Studies.

Administrative centre

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T +358 9 4744 8640; F +358 9 4744 8338

The MDC was established in 1984 in the Department of Epidemiology of the National Public Health Institute (KTL) in Helsinki, Finland. KTL had local and international experience in cardiovascular disease epidemiology, but had never been involved in the coordination of data from a multinational project. The initial skills required for its tasks were acquired quickly through visits to places that already had such experience. Visits by consultants to the MDC assisted with the further development of skills. Particularly helpful was the collaboration with Dale Williams and his co-workers then at the Collaborative Studies Coordinating Center at Chapel Hill, North Carolina.
Personnel

In the beginning, the MDC staff consisted of the Chief (epidemiologist), an epidemiologist, a statistician, a database administrator and a secretary. It soon became clear that while more resources were needed for data management and statistical computing, the need for medical and epidemiological expertise could be filled by experts from the Steering Committee and the MCCs. For the next fifteen years, the number of full-time staff at the MDC varied between four and seven persons. Crucial for the performance of the MDC was close collaboration with the MCCs, the Quality Control Centres, the Management Centre and the Steering Committee. Collaboration with the MCCs was not limited to the preparation and transfer of the study data. Numerous visits, lasting from a few days to several months, were made to the MDC by experts from the MCCs to work on statistical computing, planning and writing of the Project’s reports and publications. Also important was the careful work of many MCCs in checking the MCC specific statistical computing which the MDC had undertaken for the collaborative reports and publications.

Funding

The MDC was established by a contract between WHO and KTL. Although it was projected that the MDC would be needed for 15 years, the contracts had to be renewed annually. The first contract stipulated that the costs would be divided roughly fifty-fifty between the two parties: KTL was to provide two persons, an office and computing facilities, while WHO provided a fixed amount of money. The WHO contribution remained at the same level throughout the 1980s. However, soon after the start, the effective contribution of WHO decreased by a third because of exchange rate fluctuations. KTL responded by providing an additional full-time person in 1988. In the early 1990s, the financial contribution from WHO gradually ceased, and for six years the main source of funding outside KTL was the National Heart Lung and Blood Institute in the USA. In 1996–99, the time of the last bits of data transfer, the final quality assessments and the preparation of the final results, the main funding outside KTL came from the European Union through its 4th framework research grant (BIOMED). See Acknowledgements.

Continuing activity

The unit of KTL established for the MDC is now called the International Cardiovascular Disease Epidemiology Unit. Its main activities include:
further analysis of the MONICA data
running the Data Centre for the EU-funded MORGAM study, in which cohorts examined by MONICA and some other risk-factor surveys are followed-up for cardiovascular diseases. A subcomponent of the study is a nested case-cohort study on genetic issues
planning of coordinated population risk-factor surveys for European countries.

Key personnel

References
MONICA Web Publications are also accessible on the Monograph CD-ROM
2. MONICA Quality assessment reports and data books were published at http://www.ktl.fi/publications/monica/. MONICA Web Publications 2–18.
4. At the time of publication of this Monograph, the full archived data are still confidential. Their use is subject to the MONICA publication rules, which are available in the MONICA Manual Part I: Description and Organization of the Project. Available at http://www.ktl.fi/publications/monica/manual/part1/i-2.htm. URN: NBN:fi-fe19981148. A subset of MONICA data is available on the Monograph CD-ROM.

Kari Kuulasmaa

#8 MONICA Quality Control Centres (MQCs)

MONICA Quality Control Centres (MQCs), were the centres nominated by WHO in consultation with the MSC to provide expertise on specified areas of the core project. There were four Quality Control Centres with specific tasks. The Centre for Health Services was not established until near the end, while the other three were set-up at the inception of MONICA and had more in common. At first they were concerned with training, testing and external quality control—circulating test materials to centres to ascertain and monitor their performance. Later they were also concerned with the quality of collaborative data arriving in the MONICA Data Centre and with analysis and publication of the results. The latter tasks were also a concern for the groups that were established to look at the quality of data for other factors such as blood pressure, obesity and smoking. Because there was no external quality control of these items, they were not the concern of formal MQCs. Internal quality control was one of the responsibilities of the MCCs. See MONICA Quality assessment reports (1) which give an idea of the range of quality assurance issues that were addressed in MONICA. See also #12 Quality Assurance, sections on specific data items and #88 MONICA Memos, which show how many external quality control exercises

- training and testing were essential for successful monitoring of trends
- event registration, ECG coding, and lipid measurement were the initial concerns
- training and testing material (external quality control) were possible for these
- as data became available, quality assessment groups addressed other issues
took place, particularly in the early years of MONICA. Also see relevant parts of the MONICA Manual, such as Part IV, sections 3 and 4 (2, 3).

The terms of reference of the MQCs are listed together at the end of this section. Some centres had terms of reference that were specific to them. These are listed first. The aims and terms of reference are edited from MONICA Manual Part I, Section 2 (4).

A. MONICA Quality Control Centre for Lipid Measurements

WHO Collaborating Centre for Blood Lipid Research in Atherosclerosis and Ischaemic Heart Disease (usually known as the WHO Lipid Reference Centre)
Laboratory for Atherosclerosis Research
Institute for Clinical and Experimental Medicine (IKEM)
Videnska 800, PO Box 10
14000 Prague 4, Czech Republic

Aim
To ensure comparability of data collection in the MONICA Project by testing the performance of centres in lipid measurements.

Specific terms of reference
In close cooperation with the MSC and MMC, the Prague Centre will provide the following services:

1. Procure quality control pools for lipid measurements at the MCCs.
2. Establish and execute a reference programme for testing the total cholesterol, HDL-cholesterol and thiocyanate methods.
3. Ensure comparability at regular intervals against the WHO Collaborating Centre for Blood Lipid Standardization at the Centers for Disease Control, Atlanta, Georgia, USA.

Key personnel
*Responsible Officer:* Rudolf Poledne. *Former Responsible Officer:* Dušan Grafnetter.

B. Quality Control Centre for ECG Coding

National Institute of Cardiology
IX Haman Kato Ut 29
PO Box 88
1450 Budapest, Hungary

Aim
To standardize the interpretation of ECG according to Minnesota coding in order to improve diagnostic performance in assigning MONICA ECG categories.

Specific terms of reference
In close cooperation with the MSC, the MMC and the MQC for Event Registration, Dundee (Dundee Centre), the MONICA Quality Control Centre for ECG Coding, Budapest (Budapest Centre) will provide the following services:

1. Preparation of standard sets of ECG tracings for distribution to centres to assess differences in ECG coding. Official MONICA reference codes will be established in consultation with the Dundee Centre using the algorithm produced by the Dundee Centre.
2. Reports, including statistical analysis and commentary, will be prepared and circulated. The attention of each centre will be drawn to their weak points and suggestions for improved performance will be put forward.
3. The Budapest Centre will provide the official Minnesota reference codes for the ECG tracings included in the sets of specimen case histories elaborated by the Dundee Centre and will agree the official MONICA categories with Dundee.

4. The Budapest Centre will provide consultation services and organize training courses in ECG coding as needed and appropriate.

5. The Budapest Centre will maintain a programme of standardization for its own ECG coding activities with the Minnesota Coding Laboratory at the University of Minnesota, Minneapolis, whilst such a link remains in existence, but will also establish an external panel of expert coders, or task force, that will provide and code test material and standardize the Centre.

**Key personnel**

*Responsible Officer:* Peter Ofner. *Former Responsible Officer:* András Mádai.

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**C. Quality Control Centre for Event Registration**

Cardiovascular Epidemiology Unit
Ninewells Hospital and Medical School
University of Dundee
Dundee DD1 9SY, Scotland

**Aim**

To standardize the coding and classification of coronary and stroke events according to the MONICA Protocol in order to improve comparability and stability within and between centres, thereby maximizing the chances of detecting true time trends in event rates and minimizing the likelihood of spurious trends.

**Specific terms of reference**

In close cooperation with the MSC, the MMC and the MQC Budapest, the Dundee Centre is responsible for the following areas:

1. Preparation and circulation of sample case histories and other material covering both coronary and stroke events, to be followed up with general commentaries and specific reports.
2. Developing an operational definition for coronary and stroke events leading to diagnostic algorithms and, where appropriate, computer programs based on these.

**Key personnel**


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**D. Quality Control Centre for Health Services**

Department of Public Health
University of Western Australia
Western Australia 6907, Australia

**Aim**

To develop methods for the collection and quality assessment of standardized data on the provision of health services and selected aspects of medical and surgical care for the management of cardiovascular disease in MONICA Collaborating Centres.

**Specific terms of reference**

In close cooperation with the MSC, MDC, MMC and MQC for Event Registration, the Perth Centre is responsible for the following areas:
1. Developing and testing, in consultation with the MONICA Data Centre and the Steering Committee, the data instruments to ensure collection of comparable data for health services assessment within the WHO MONICA Project.

Key personnel

Common terms of reference, applying to more than one MONICA Quality Control Centre
1. Respond to queries on their area of expertise, provide consultation services and organize training courses and workshops where appropriate.
2. Provide periodic summary reports on the performance of the various centres drawing attention to their weak points and making suggestions for improvement.
3. Assist the MMC in taking appropriate action when the performance of an individual centre is unsatisfactory.
4. Present status and progress reports at regular intervals to the MSC.
5. Respect confidentiality of all data received from MCCs.
6. Communicate directly with individual MCCs on technical matters, or through the MONICA Memo system.
7. Collaborate with the MDC, MSC and MCCs in preparing reports on the quality of event data sent to the MDC and its interpretation.
8. Assisting in the revision of the appropriate section of the MONICA Manual and in the preparation of manuscripts.

References
MONICA Web Publications are also accessible on the Monograph CD-ROM

Hugh Tunstall-Pedoe

#9 MONICA Reference Centres (MRCs)

MONICA Reference Centres dealt with optional studies carried out within the framework of the WHO MONICA Project. See #43–#49. They coordinated and advised on their specific areas of expertise as follows:

- acted as resource centres in areas in which they had special expertise or interest
- helped to develop common protocols and provide a focus for the relevant optional studies
- coordinated any collaborative studies and planned any joint analyses
- advised their collaborators on any methodological or quality control problems whenever necessary
- organized data management for the respective optional study
- kept the MMC informed through six-monthly reports

- initiatives to collaborate on subjects and items beyond the MONICA core
- difficult or expensive to measure, or not cross-culturally standardized
- often inadequately resourced
- MONICA’s Cinderella subjects, but some successes (see #43–#49)
followed international developments in their respective fields, helped with necessary contacts with other related studies and advised centres on possible additional activities in the field in question.

This listing is taken from the latest MONICA Manual. Some of these reference centres are no longer operational, others are still working on data analyses and publications and some have changed their provenance. In the absence of central funding it is not surprising that they did not all succeed in fulfilling their terms of reference and some changed their sites and responsible officers over the years. See #43–#49.

**MRC Nutrition (MRC-NUT) (See #44)**
Department of Chronic Diseases and Environmental Epidemiology National Institute of Public Health and the Environment PO Box 1 NL-3720 BA Bilthoven, The Netherlands

*Responsible Officer:* Daan Kromhout. *Former Responsible Officer:* Guy De Backer (Ghent), Pirjo Pietinen (Helsinki).

**MRC Vitamins and Polysaturated Fatty Acids (See #45)**
Vitamin Unit Institute for Biochemistry and Molecular Biology University of Bern Bühlstrasse 28 3000 Bern 9, Switzerland

*Responsible Officer:* Fred Gey. Now transferred to Alun Evans (Belfast).

**MRC Physical Activity (MOSPA) (See #47)**
Behavioral Epidemiology and Evaluation Branch Division for Health Education Centers for Disease Control Atlanta, Georgia 30333, USA

*Responsible Officer:* Deborah Jones. *Former Responsible Officer:* Daniel Brunner (Tel Aviv), Kenneth Powell, Diane Jones (also CDC, Atlanta).

**MRC Psychosocial Substudy (MOPSY) (See #46)**
Office of Chronic Diseases, WHO Regional Office for Europe 8 Scherfigsvej DK—2100 Copenhagen

*Coordinating Officer for Optional Studies:* Siegfried Böthig (Zwickau, Germany).

**Hugh Tunstall-Pedoe**

**MRC Drugs (MRC-DRG) (See #48)**
Bremer Institut für Präventionsforschung und Sozialmedizin (BIPS) St Jürgen Str. 1 D—2800 Bremen 1

*Responsible Officer:* Eberhard Greiser. *Former Responsible Officer:* K Øydvin (Oslo).

**MRC Haemostatic Factors and CHD (MRC-HFC) (See #49)**
Division of Epidemiology The Queen’s University of Belfast Mulhouse Building Grosvenor Road Belfast BT12 6BJ

*Responsible Officer:* John Yarnell. *Data Coordinator:* Evelyn McCrum (Belfast). *Laboratories:* Gordon Lowe, Ann Rumley (Dept of Medicine, Glasgow), Michael Brown (Dept Haematology, Frenchay Hospital, Bristol).

*Data Centre:* Ursula Härtel, GSF-MEDIS Institute, Neuherberg-Munich.
#10 Recruitment of Populations

**Requirement for recruitment**

Trends in morbidity, mortality and risk factors in one population cannot necessarily be extrapolated elsewhere. Following the American experience, the World Health Organization MONICA Project was set up to monitor what happened in many different populations in order to elucidate the underlying patterns. What had happened in the United States might be atypical. Realization of what was occurring there had come too late to make critical observations at the onset of the decline (1). MONICA needed data from different populations and countries at different stages of the rise and fall of cardiovascular disease, and particularly coronary heart disease, mortality. See #1 Background to the WHO MONICA Project. It was hoped to recruit populations with differing levels of coronary and stroke mortality, where predicted trends were increasing in some and decreasing in others. Therefore, geographic, cultural, social and material diversity of populations was to be welcomed.

**Constraints on recruitment**

To produce usable data however, there were constraints on which populations could be considered. The populations had to be relatively stable, living within well-defined geographic or administrative boundaries. Medical services for coronary heart disease and stroke had to be available within the area, and sufficiently advanced to provide proper diagnostic facilities to facilitate case-ascertainment of acute events. MONICA registers were to use existing diagnostic data on non-fatal events, and medico-legal data on fatal events. While cardiovascular clinical expertise was needed within the population, the MONICA Collaborating Centre (which could be based at some distance from it) also needed to have access to expertise in cardiovascular epidemiology in order to understand and conform to the common protocol, to be able to set up disease registers and to mount population surveys. Population demographic and routine mortality data for the population concerned had to be available.

Unfortunately these requirements, a consequence of the need to validate diagnoses and calculate event rates and trends, made recruitment of populations from developing countries problematic. In the early 1980s, most of the world’s population was not living in countries that could provide death certificates or population denominator data needed for the calculation of mortality statistics (2). This, as well as the need for long-term commitment of resources, explains most of the geographical distribution of the eventual MONICA populations, see graphics G1 and G2. There were no populations from South America or Africa, and few populations from Asia. The lack of populations from North America had other explanations. Strongly involved in the early planning of MONICA, the National Heart, Lung and Blood Institute (NHLBI) ran an exploratory study, the Community Cardiovascular Surveillance Program (CCSP), in the USA and then continued with a parallel but different study to MONICA, the Atherosclerosis Risk in Communities, ARIC study (3).

**Funding**

The most fundamental requirement for recruitment (although never stated in the MONICA Protocol) was that the potential MONICA Collaborating Centres, which volunteered the populations that interested them, had to be self-funding. The World Health
Organization funded coordination, but not registration or population surveys within the populations concerned—see population pages #51–#83 where sources of funding are listed. Although 10-year funding was not necessarily always guaranteed at the start, recruitment was only feasible if that possibility had not been definitively excluded. Unlike a centrally funded drug trial therefore, where almost every detail can be rigidly enforced, MONICA was always an association of independently funded investigators who had agreed to work together. MONICA would not have been possible without the prior existence of many experienced groups around the world with an interest in the same problem, able to make the long-term commitment and to find local funds. Some recruits were relatively inexperienced but brought with them their enthusiasm to learn and participate as well as stable funding.

How big a population—Reporting Units and Reporting Unit Aggregates

Much time was spent in the early stages discussing population sizes. It was calculated that in order to establish trends with a satisfactory degree of precision over a 10-year period, a candidate population would need to be experiencing 300 coronary deaths a year in men in the target age-range of 25–64. This target was found to be a problem. It meant a large population even where disease rates were high, and an enormous one where they were low, and implied that trends in coronary disease in women and in stroke would not be measurable. On this basis, few populations would have qualified. However, if trends in rates were larger than expected, they would be detected with smaller numbers. The number was later changed to 200. The Data Book shows that although many MONICA populations were below even that target they still made a contribution (4).

Later a different statistical viewpoint prevailed. It was not necessary for trends within each population to be measured with great precision. For testing hypotheses across populations it was desirable to have many populations that were as heterogeneous as possible—differing from each other, but internally homogeneous. In order to produce large enough populations some MONICA Collaborating Centres had designated populations that were made up of different components. It was decided that each of these components should be identifiable as a Reporting Unit (RU), and coded thus on the relevant data records. A subsequent decision could be made as to how these were put together as Reporting Unit Aggregates (RUAs) (5). Precision of estimated trends within populations was therefore not the real issue for MONICA collaborative analyses. However, it could be for individual investigators in small centres who might spend ten years recording trends in event rates without ever knowing precisely which way they were going (see graphic G15 which shows estimated trends and 95% confidence intervals for coronary-event rates). This problem was particularly true for trends in coronary disease in women and for trends in stroke.

How many populations?

In the very early planning stages it was envisaged that MONICA would consist of perhaps 10–15 populations, however, it finished up with two to three times that number. Such a response was an embarrassing success for the World Health Organization as it made MONICA a more costly study than had been planned. Looking back, it is clear that 10–15 populations would have been a great improvement on the previous American experience, but with each population being one data point, the number of these points would have been less than ideal for the regression analyses that were eventually used, although number is not the only criterion. (Compare the hypothesis testing analyses in this Monograph for coronary events: 38 points and for stroke 15 points. See graphics G69–G77.)
Recruits on probation: candidate MONICA Collaborating Centres

In the early days, suitable populations, with the promise of funding, were welcomed to MONICA through their Principal Investigators. However, they still had to qualify by providing results of pilot or feasibility studies and a local Manual of Operations translated into English (see #19 Other Documents Used in MONICA). After some centres had begun registration and others had yet to do so, the Council of Principal Investigators decided that to qualify, coronary-event registration had to be started by October 1984. This meant that the full calendar year with which the latest starters began their trend analyses for coronary events was 1985, see graphic G8. Full participants in MONICA who continued to fulfil the requirements for continuing participation were designated MONICA Collaborating Centres. Fellow travellers, who ran in parallel but did not qualify in time to be included in the Project, or lapsed from full participation, were designated Associate Collaborating Centres. These funded their own participation at Principal Investigator Meetings and their data were not centrally analysed. This Monograph is mainly concerned with those MONICA Collaborating Centres that provided sufficient data to help test the original MONICA hypotheses on trends.

References


Jaakko Tuomilehto, Zbyněk Piša, Hugh Tunstall-Pedoe

#11 Communications in MONICA

Introduction

MONICA investigators had to communicate and transfer data and manuscripts across the world by various means. Looking back, it is difficult to imagine MONICA being successfully completed without the means of communication that developed as the project progressed.

Communication groups

Within MONICA there was a worldwide network of communications across the study structure, not all the elements of which are shown in the organization chart in #3. The different groups were:

- the Council of Principal Investigators (CPI)
- the MONICA Steering Committee (MSC)
- Manuscript Groups, and others.

MONICA Collaborating Centres (MCCs), the MONICA Management Centre (MMC), the MONICA Data Centre (MDC) and MONICA Quality Control Centres (MQCs) were in frequent, often daily communication with each other, back and forth.

- a research network which created an international ‘MONICA family’
- over two decades experienced and exploited the communications revolution
- e-mail, FAX, and the Internet carried an otherwise under-resourced international project to completion
- MONICA Investigators pioneered the new technologies in their own institutions
Forms of communication
These ranged from formal meetings and working visits to telephone conferences and MONICA Memos (see below).

Early formal conferences of investigators
The WHO MONICA Project began with a series of meetings of would-be investigators, planned months beforehand, with written invitations, agendas, conference documents, minutes and conference reports. These could not take place more than once or twice a year. Planning communications came by normal surface mail and airmail. Large institutions had TELEX machines but these were rarely used. Telephone use was limited by its cost. Some people were happy to receive international calls but not to initiate them.

MONICA Steering Committee meetings
The meetings of Principal Investigators were large, very costly and infrequent. It was decided to set up a MONICA Steering Committee that would meet every few months. It had a designated membership of continuing and rotating members. It met frequently during the early stages of MONICA, and less frequently thereafter. Agendas, documents and minutes came by mail. Meetings were costly and difficult to arrange. The MONICA Steering Committee had had 29 formal face-to-face meetings by the end of 2001 but these had become increasingly infrequent, because of the expense and, conversely, because of the advent of cheaper methods of communication.

Telephone conferences
With reductions in the price of telephone calls the MONICA Steering Committee began to arrange monthly or two-monthly telephone conferences. The main difficulty was arranging times and dates when everyone could participate—the Committee covers many different time-zones. By the end of 2002 the MONICA Steering Committee had held 105 telephone conferences.

MONICA Memos
The MONICA Management Centre in Geneva introduced a system of MONICA Memos (MNM) to circulate and request information. The contents varied, but they always had a covering letter from the Chief of the CVD Unit and an opening statement as to what action was required, by what deadline, and where the response was to go. Planning and sending a MONICA Memo and getting a reply took several weeks at first. There were comments about delays at MONICA Meetings. Nonetheless, the MONICA Memo system was invaluable and over 400 were circulated between January 1983 and December 2002. A Memo could vary in length from one sheet of A4 paper to a large set of tables or a draft paper for approval. Reproduction and distribution of MONICA Memos was a major function of the Management Centre and could not have been assumed by anyone else. The covering letter from WHO gave them official status. They were not to be ignored. Some were distributed widely to a general mailing list while others contained unpublished data for Principal Investigators alone. (See #88 MONICA Memos and also the Monograph CD-ROM part 2.) There were eventually three varieties: A—confidential, B—not confidential, and C—electronic (see below).

FAX
After the mid-1980s, MONICA entered the electronic age. “Do you have access to a FAX machine?” became a routine question. Initially this meant seeking help from another department, hundreds of metres away in the same institution, or through a post-office or shop. Output was often a slippery piece of paper,
Sorting E-mails on the Monograph, Dundee June 2001
difficult to write on, darkening or fading when exposed to daylight, and documents could be unreadable even when newly received. Later every small department got its own machine.

E-mail
The MONICA Steering Committee started using electronic mail in 1987 and has circulated thousands of messages since then. MONICA investigators were often way ahead of academic or medical colleagues in this respect. Difficulties with ‘attachments’ were initially very common and unfortunately still occur. For eastern European centres where ordinary mail could take weeks, this was a major advance, starting often through amateur networks.

The World Wide Web
The final step in rapid communication occurred when the MONICA Data Centre in Helsinki started a website for the WHO MONICA Project in 1996: http://www.ktl.fi/monica/. The public website describes and identifies the project, listing its sites and key personnel and MONICA publications. Linked to it however are password-protected pages which contain much of the ongoing business of MONICA. The MSC page contains minutes and agendas of telephone conferences and documents for discussion. MONICA manuscript groups had their own web pages for draft documents. Even the data analyses performed in the MONICA Data Centre were published on the manuscript groups’ web pages. For example, the graphics in this Monograph were developed between Helsinki and Dundee. Updated versions were placed on an internal web page from Helsinki and an e-mail message sent to Dundee where they were downloaded and commented upon by e-mail. This could be done several times in one day. Differences in time-zone and working hours were often advantageous, with late-night comments from Dundee acted on in Helsinki while Dundee was at breakfast. The latest MONICA Memos have been distributed through the web.

MONICA collaborators, through the cross-fertilization of ideas, and demands of the project, have been ahead of their national colleagues in using new technology. However, the price paid for rapid communication of information is that there is too much of it from different sources, and documents can be overlooked. “I have not received it”, is the face-saving plea of a busy colleague sent a FAX or e-mail, now buried. Recent communications however, show that some MONICA Collaborating Centres still have notepaper with their TELEX address proudly displayed!

Hugh Tunstall-Pedoe
Quality Assurance

A major concern for any large-scale, long-term multi-centre collaborative study is to collect data of appropriate quality that is highly comparable across the many participating centres that are collecting the data and over the several years of the study’s duration. This issue was especially important for the MONICA Project as it was being planned for 30–40 MONICA Collaborating Centres (MCCs) in 24 countries over four continents with even more numerous, often separated populations under study. It involved data collection activities from three separate screening activities over a 10-year period, plus those required for other important data components such as coronary and stroke-event registration, monitoring of coronary care, and collection of routine mortality and demographic information.

To address this fundamental issue, the MONICA Project created and operated a carefully constructed Quality Assurance programme. This programme was developed by the MONICA Steering Committee (MSC) and was implemented with considerable energy by the MONICA Management Centre (MMC), the MONICA Data Centre (MDC), the MONICA Quality Control Centres (MQC) and selected members of the MSC. Quality Assurance was based on:

- the use of standardized data collection methods and procedures
- training of the data collection and data processing personnel in the use of standardized methods
- quality control at various stages of data collection and processing, and at various levels of the Project
- retrospective assessment of the quality of the data that was eventually attained and the documentation of shortcomings and centre-specific features in the data.

The data collection standards as well as instructions for the training and internal quality control in the centres are described in the MONICA Manual (1). Three MONICA Quality Control Centres were created at the start. Each was responsible for training MCC data collection personnel and for assisting the MSC with monitoring the performance of the individual MCCs in the relevant areas. The three MQCs were:

- MONICA Quality Control Centre for Lipid Measurement, responsible for the quality of the total cholesterol, HDL-C and triglycerides measurements,
- MONICA Quality Control Centre for Event Registration, responsible for the quality of the registration and coding of coronary and stroke events, and
- MONICA Quality Control Centre for ECG Coding, responsible for the quality of the coding of electrocardiograms.

(See #8 MONICA Quality Control Centres (MQCs).)

After the experience of the initial population surveys, two training seminars were organized for those in the centres responsible for the local training of survey teams. These were held in Helsinki in 1991 and in Gargnano, Italy, in 1993.

The MSC assessed the overall quality of the data collection process and the transmission of data to the MDC on a routine basis. These reviews covered a number of issues. Scores on individual items and overall scores were reviewed with the MQC leadership at MSC meetings.
The quality of the data attained, together with a description of any shortcomings and centre-specific characteristics, were documented separately for each major data item in MONICA Quality assessment reports. These were produced periodically, and some of the problems identified could still be remedied. The final MONICA Quality assessment reports were published on the World Wide Web (2). They are an invaluable source of information for anyone analysing the MONICA data.

Perhaps most important was the fact that a carefully constructed and implemented Quality Assurance programme was used by the MONICA Project. This programme received constant ongoing attention from the MSC and all the central agencies and committees. Further, it was supported by the MCCs in their efforts to contribute high quality, useful data.

References
MONICA Web Publications are also accessible on the Monograph CD-ROM
Quality Assurance is so pervasive in MONICA that it is invidious to name specific documents. It is referred to in specific sections of this Monograph but see also:


Dale Williams, Kari Kuulasmaa

#13 Ethics and Confidentiality

Introduction
In the 1980s ethical issues were not of major concern to MONICA as it was following well-established procedures. Unlike recruitment for trials of powerful new drugs or procedures, the physical risk to people involved in MONICA’s disease registration or population surveys was immeasurably small. Even so, there were ethical issues of consent and confidentiality. MONICA investigators had to satisfy local ethical requirements for research in each population in which they worked. These requirements were sometimes illogically inconsistent in different countries. Recent attempts at international standardization through measures such as the European Convention on Human Rights may be beneficial in the long-term but much will depend on how they are interpreted. Just now it would be difficult to initiate a new MONICA Project in many former participating countries because of doubts about what newly framed legislation on confidentiality, medical records, and civil rights actually means. The issues involved in population surveys and in coronary or stroke event registration will now be considered separately.

Disease registration
In order to calculate trends in event rates and survival, the investigator must be able to include information on all the possible events that come to the attention of the medical and medico-legal systems. This means obtaining access to case notes, pathology and biochemistry reports, both in hospitals and in the community. These need to be merged with information from death certificates and death records, eyewitness accounts of sudden deaths and post-mortem reports. In the case of ‘hot pursuit’ some information will be obtained directly from living patients, with permission given face to face. In the case of ‘cold pursuit’ and for fatal cases, this is not practical. (See #20 Registration of Coronary Events, Hot and Cold Pursuit.) Registration and the linking of records
in MONICA were usually approved by privacy and ethical committees who were satisfied that the researchers were of good standing, would keep the information securely, and use it only for medical research. They could even make it a condition that no direct contact be made with living patients or relatives. Medical records belonged to the medical and medico-legal organizations concerned. Newer ideas implying that records belong to the patient and may not be used for any purpose without individual written permission threaten the completeness of disease registration. Patients refusing permission would be undermining the need for comprehensiveness. Results would be biased and incomplete. Refusal of some would tend to devalue the remaining contributions of the majority who did take part.

Population surveys
These cannot be done without the explicit cooperation of the participant. Ethical concerns involve the researchers’ access to the sampling frame, and the way in which the original written invitation is phrased. Does it accurately state what is involved? Does it make unjustified promises of personal benefit to the participant? What follow-up recruitment methods are justified if there is no response? On arrival at the clinic the participant had to have a full explanation and give written consent to the survey procedures. This included venepuncture for blood specimens. Potential problems here were what to do if any of the individual findings was seriously abnormal and who, if anybody, should receive a report. Non-participation, or non-response is a well-recognized problem in such surveys. (See #29 Recruitment and Response Rates.)

Data management
Individual medical or risk-factor information is necessary for the event registration and population survey components of MONICA. Records of individuals are maintained, although the analyses are carried out on whole groups. It is essential to maintain the individuality and integrity of each record without compromising confidentiality. This is usually done by keeping the MONICA medical information entirely separate, but with a unique personal number, which can be cross-linked with a confidential file elsewhere containing identification information such as names and addresses. The latter is needed for several reasons. One is that the research is much more powerful and cost-effective if it involves ‘following-up’ participants for their future mortality and morbidity. The researcher then needs to be able to link MONICA records with subsequent hospital or death-certificate data. This cannot be done without personal identifiers. It is also important to be able to check whether records have been inadvertently duplicated. In addition, research participants have the right to know what information is held about them on computer.

MONICA, in distributing anonymous records through the MONICA Database for further analyses by collaborators, has taken care to remove potentially over-specific information. Actual birth-dates were removed from the records before they were distributed, although it seems inconceivable that anyone would seriously wish to identify individuals on that basis.

Many MONICA Investigators, with permission, took specimens of urine, blood and sometimes other tissues for immediate analysis, but then stored what was left for further analyses of possible new risk factors in the future. Some research ethics committees now want researchers to specify exactly what tests are to be done when a specimen is requested, which would limit such activity. A particular problem arises with specimens containing DNA, unique genetic material, a problem now facing many researchers and research committees. The DNA profile of an individual has implications for their blood-relatives as well.
as themselves. There are also potential problems of ‘ownership’ of biological material which might have commercial implications, such as patent rights.

**Conclusion**

MONICA investigators conformed to best practice in their own countries. In the two decades of the MONICA Project the MONICA Steering Committee and MONICA Data Centre have not been made aware of any breaches of confidentiality, or of ethical complaints arising from this huge study.

Increasing sophistication, both of medical research and of the general public have made issues of ethics and confidentiality increasingly prominent. It is important for the future that non-commercial research in public health for the public good such as MONICA is not prevented, or seriously frustrated, by over-zealous legislators, by over-promotion of individuals’ rights without concern for their responsibilities, or by sensational publicity leading to a breakdown of public trust. Much will depend on the good sense of the public and on such research continuing to be seen as for the public good rather than private gain.

**Alun Evans, Hugh Tunstall-Pedoe**

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**#14 MONICA and the Prevention of Cardiovascular Disease**

**Questions for prevention**

The ultimate aim of the MONICA Project was to serve prevention. It was designed to cast light on crucial questions from the 1980s whether trends in mortality are more influenced by primary prevention (attack rates) or by treatment (case fatality). Are trends in attack rates in the population driven by changes in risk factors—a key question in primary prevention?

Already during the design of the project a number of problems were encountered. These were related to our ability to measure changes both in risk factors and in disease rates. These questions concerned sample sizes, age groups and possible time-lags. Although these problems surfaced again in the analysis of the results, the MONICA Project has nevertheless provided significant answers to its original questions.

**Answers and new questions**

According to the results, both primary prevention and treatment influence mortality trends. The pattern varies in different populations. A high proportion of pre-hospital deaths puts great emphasis on primary prevention. Trends are influenced by risk factors—allowing for some time-lag. The degree to which risk-factor changes can explain trends remains, unfortunately, somewhat unclear. Like all research, MONICA provided answers, but raised many new questions. As a result, the project is likely to inspire further research into prevention.

**Other benefits**

The WHO MONICA Project has served global cardiovascular disease (CVD) prevention in other important ways, but indirectly. MONICA has been a model for how a huge multi-component, multinational project can be implemented and managed, how standardized data can be collected, data analysed, communication organized, and so on. Further, MONICA became, as one of its founders predicted, a gold standard ‘model for good housekeeping’ in monitoring trends in CVD rates and respective risk factors. Countries and programmes that had
nothing to do with MONICA use and refer to ‘MONICA methodology’ in their work. MONICA has shown the way in CVD monitoring, a cornerstone for prevention.

**Growing global burden of CVD**

During the twenty years that MONICA was carried out, a significant change took place in the global burden of CVDs. When MONICA was started, CVDs were predominantly seen as the burden of industrialized countries. Indeed, most of the MONICA centres were in that part of the world. At the end of the MONICA period, estimates showed that CVDs had rapidly increased in the developing world, and that the epidemic continues to increase. Today the majority of the CVD deaths in the world are in developing countries. Every third death in the world is cardiovascular (1). Coronary heart disease is the number one killer in the world. CVDs are increasingly attacking economically disadvantaged countries and population groups, thus contributing to poverty and hindering economic development.

**CVD prevention—key for global health**

Thus, CVD prevention is a crucial issue of contemporary global public health. Fortunately, as MONICA results show, quite dramatic reductions in CVD attack rates are possible. The greatest reduction was by as much as 6.5% per year over a 10-year period in North Karelia, Finland. This is a province in which systematic long-term prevention has been implemented.

Our challenge is not merely to predict and to monitor the trends, but to influence them. Even modest changes in CVD trends can have a huge public health impact. And many MONICA centres show that quite substantial changes can take place in ten years—both up and down. These kinds of changes have nothing to do with genetics; they are the result of environmental changes, and especially of lifestyle changes. Prevention is possible and it pays off.

**MONICA’s place in the history of CVD prevention**

The WHO MONICA project has without any doubt significantly contributed to global prevention efforts. This has occurred because of its scientific contributions, and through the provision of a good foundation for future monitoring and surveillance efforts. One challenge for prevention is to create meaningful, coordinated global efforts to reverse the unfavourable trends that we see in a large part of the world. The focus should be on broad instructions to reduce the numbers of people affected by the few well-proven risk factors that relate closely to certain lifestyles. This calls for global leadership by WHO, and strong collaboration between governments, public health experts, and other partners.

**Reference**


**Pekka Puska**

Director, Noncommunicable Disease Prevention and Health Promotion, World Health Organization, Geneva. Previously Principal Investigator of FINMONICA 1982–87, first Chair of MONICA Steering Committee
first met Zbynek Piska, MONICA’s godfather, in 1969 in the office of Professor Jerry Morris at the London School of Hygiene and Tropical Medicine. Setting up a heart attack register was one of Jerry Morris’s dreams, foreshadowed in his book on Uses of Epidemiology (1). It was finally happening thanks to the European Heart Attack Registers. These were being coordinated by Zbynek Piska, the officer responsible for chronic diseases at the World Health Organization Regional Office in Copenhagen. I had been recruited, as a young trainee cardiologist, to set up a register in the London Borough (suburb) of Tower Hamlets. The dream was coming true. We needed a community perspective to explain why population mortality rates continued to rise when coronary care units (CCUs) were being championed as halving heart-attack mortality.

Months later I attended a World Health Organization Working Group Meeting in Copenhagen. Zbynek Piska told me that, as the English-language participant, I was to write up the proceedings—in WHO terminology I was the Rapporteur. I had brought my family with me for a holiday. I never did so again.

Diagnostic criteria for definite myocardial infarction were based on a WHO document of 1959 (2). This provided, with illustrations, two electrocardiographic criteria: development of new Q waves, and evolution and disappearance of an injury current in three stages. A footnote said that an injury current was not necessary if new Q waves were observed. I questioned whether evolution of an injury current was also sufficient—otherwise it was illogical and redundant. Nobody knew. I summoned up courage and inserted ‘and/or’ between the two criteria where they have remained ever since (3, 4). Diagnostic criteria are not just descriptions—they have to be watertight and to be able to classify potential cases consistently, something often forgotten even now (5).

Quality control
At the next meeting I suggested circulating test case-histories, to see whether coding was consistent. I was asked to do so. Results showed major disagreements on certain items, and failure by some participants to understand why these were included. One group claimed that all their coronary deaths occurred in hospital. It was a minority in the other centres. The explanation given by the group was that nobody was dead until a doctor said so: there were no doctors outside the hospital. Jerry Morris chaired this meeting. He insisted that we start again using only data collected after key items had been more specifically defined. However, earlier data re-emerged in the final publication. Looking back now it was rather primitive—bundles of incomplete record forms being sent to and fro across Europe. Although we had defined definite and possible myocardial infarction, the latter including some very borderline cases, results were pooled in the final analyses. Zbynek Piska, by this time in Geneva, asked me to write a chapter on methods for a monograph on Myocardial Infarction Community Registers (3). I did so, stating what had worked, what had not, and identifying problems. The chapter was acknowledged, but the monograph appeared without it. I was told later that my chapter was “not quite what was wanted”. By this time I was working on another WHO study with coronary end-points, the European factory study, with Professor Geoffrey Rose (6). I published my critique of heart attack registers in a cardiology journal, its title honouring Jerry Morris (7).

Preparations for MONICA
In 1979 Zbynek Piska asked me to send him reprints of this critique to be used as a working document for a small meeting that followed the Bethesda Conference on the Decline of Coronary Heart Disease Mortality (8). The plan was to
revive heart attack registration so as to study trends over time. That year I spent several weeks in Minneapolis at the then Laboratory of Physiological Hygiene, Stadium Gate 27, where the Minnesota Heart Survey was being launched to monitor trends in coronary disease and risk factors. This was the home of the Seven Countries Study (9), and of Minnesota coding of the electrocardiogram (10), as well as the joint parent of Cardiovascular Survey Methods (11). Immediately after Zbyňek Písá's small meeting in September 1979 he asked me to be Rapporteur at another meeting taking place two months later in Geneva, and to draft the outline of a protocol for a study of trends by listing the subject headings in preparation for this. So began my involvement with a series of meetings leading to MONICA. Ron Prineas from Minneapolis was a consultant at these early meetings. We used the European Myocardial Infarction Community Registers (3), the Minnesota Field Survey Manual (12) and Cardiovascular Survey Methods (11) to plan the study. In 1981 I moved to Scotland and helped to initiate Scottish MONICA, fortunately for me, as England did not participate.

Development of the protocol and the name
Attendance at early meetings changed but the Chair, Fred Epstein, and the Rapporteur, I myself, did not change. There was creative tension between his ambitious wish to relate trends in cardiovascular disease to ‘changes in known risk factors, daily living habits, health care and major socioeconomic features measured at the same time in defined communities . . . ’ (13) and my wish to define what was feasible and measurable. The group discussed the title of the project. I suggested ‘determinants’ for risk factors and argued for ‘multinational’ rather than ‘international’. Zbyňek Písá had doubts about ‘multinational’ but the long title was being spelled out as Multinational Monitoring of Trends and Determinants in Cardiovascular Disease, when Tom Strasser, a Medical Officer in the CVD Unit (subsequently with the World Hypertension League in Geneva) cried, “In that case you will have to call it the MONICA Project!” The short name and the long name remained.

‘MONICA’ was a marvellous name. It was one of the first studies to be given an acronym. Others copied it. Many knew about MONICA years before we produced any results, because the name intrigued them. In 1998 during the summer’s ‘silly season’ when there was little news, press reports of the initial results of MONICA that we had presented at the European Congress of Cardiology in Vienna, mischievously suggested that there was no connection at all between coronary risk factors and coronary risk. The name MONICA was so topical for other reasons to do with the American presidency that I was able to use it to obtain very rapid publication of an article refuting the media misrepresentation (14).

Fred Epstein was a charming and accomplished Chairman. He knew that meetings could not draft documents. When we reached a controversial subject, and four different speakers had produced five opinions on what we should do, he would say “Thank you everybody. We will now move on to the next topic. We can safely leave what you have said with our excellent Rapporteur”. I would then struggle to produce a proposal that was sensible and feasible. By the next meeting former protagonists had forgotten their previous positions, and would suggest minor changes in wording. It took months of work, with visits to Geneva between meetings. I was once there to consult on psychosocial studies and measuring medical care. The WHO expert on the latter told me that we could not record quality of coronary care, because medical intervention in chronic disease generally made outcomes worse—an orthodox view around 1980, just as the extraordinary coronary care and secondary prevention revolutions were beginning. Luckily, we ignored his advice.

Ten years had made a big difference to the science of such studies. Monitoring of trends meant trying to detect small changes. Quality control was
essential. Training and testing were fundamental. I was again struggling with diagnostic criteria which, this time, were more quantitative (4), and with preparing and marking endless series of test case-histories, see #88 MONICA Memos. Early meetings of Principal Investigators were preoccupied with quality assurance, with announcing results of quality control exercises, and with coding workshops. I remember a cry from the floor once, “Quality control, quality control, I have never heard of such a study for quality control!” It was not mutiny as the centre concerned followed decisions carefully, once they were made.

**Early years**

We spent a long time waiting for results to accrue in the Data Centre in Helsinki and to pass our numerous checks. The first collaborative population survey results on risk factors were published in 1988 and 1989 (15, 16). Although there was concern about aspects of quality control and response rates, population surveys were a well-established epidemiological routine. Results from coronary-event registration, however, took considerably longer. In 1990, as head of the Quality Control Centre for Event Registration I reviewed data then available in the MONICA Data Centre in Helsinki, and reported back to MONICA Collaborating Centres in a MONICA Memorandum (17). It was ‘crunch time’ for MONICA. Data from only a handful of MONICA centres were publishable, the majority having overlooked an important protocol requirement. They had submitted only cases satisfying MONICA diagnostic criteria, not those clinically diagnosed as myocardial infarction or coronary deaths that failed the criteria. (A similar problem existed with stroke.) This meant that numbers of MONICA coronary events, if fatal, were smaller than numbers of coronary deaths in local statistics. A similar situation applied to non-fatal myocardial infarction. We needed fully coded details of all false-positives to be made available, to prove that reported cases were not being overlooked (13, 18). Round the world, MONICA Investigators had to go back several years and send in record forms for the missing false-positive cases. Everybody did so with good grace. The first cross-sectional paper on coronary events was published in *Circulation* in 1994. It was a paper with a worldwide impact and has been cited since more than 500 times (4).

**Maturity**

Following the publication of cross-sectional results came years of data accumulation, discussion of data quality, and of centres failing to meet deadlines for essential data. Some discussions were interminable and slow to resolve. After one MONICA Steering Committee meeting I suggested to the then Chair that I re-circulate the minutes from the previous year to see if anyone noticed the difference. He was not amused. Eventually we parted company or lost contact with failing centres. We were then able to concentrate on the long-term data we had, and how it should be analysed.

Finding that the *Lancet* was interested in publishing our 10-year results by fast-tracking made an enormous difference. Some MONICA papers had spent months or years with particular journals, or had received referees’ comments that disheartened the original authors, who moved on to other things. Knowing that editors were interested and waiting was a great stimulus, although the papers concerned still needed an enormous effort both in submission and in dealing rapidly with referees’ comments (19–21). Although the main results papers of MONICA were well received, a problem has always been that tables with 30 rows or more for different populations, and numerous columns, are difficult to read. Editors prefer tables to figures. Figures usually appear in black and white, too small for individual results to be read with ease. Most readers of the papers would not study the tables carefully and this would be true even of
many statisticians and epidemiologists. While preparing the main results papers for MONICA, however, we showed superb colour slides at scientific meetings. But these were too transient for the audience to identify specific populations, and were not published.

This Monograph provides the opportunity to celebrate the MONICA Project at 23 years, to make our results and data available in one place to scientists, students and teachers, and to publish our coloured graphics for general study. Publication marks the end of a classic era. MONICA was launched when individuals and funding bodies were sympathetic to a ten-year commitment to answer a major problem. We are now in an era of rapid results, ‘more bangs to the buck’, and multiple career moves. MONICA finally took over twenty years, a third of my life and proportionately more of the lives of those who are younger. MONICA investigators refer to the MONICA family with the question whether MONICA was a wife or a mistress. Either way it is improbable that we will see her again—despite many of us suspecting that twenty years of data on trends would have helped to answer many of the questions that were left unresolved.

References
MONICA Web Publications are also accessible on the Monograph CD-ROM

17. MONICA MEMO 177 of 15.02.90. Eligibility of MCCs for publication of Coronary Event Data. Internal MONICA Document distributed to all Principal Investigators. (See CD-ROM.)


*Hugh Tunstall-Pedoe*
One of the primary purposes of MONICA was to assess the validity of routine mortality data from death certificates. This is because there were concerns that trends in death rates from coronary heart disease and stroke were artificially affected by changes in reporting and coding practices, changes in the International Classification of Diseases (ICD) (see Glossary), and changes in diagnostic accuracy (1, 2). In addition, death certificate coding may vary between countries leading to artificial differences in death rates, one explanation for the so-called ‘French paradox’.

Therefore MONICA collected annual numbers of deaths, for selected causes of death by age and sex, in the study populations. The causes of death included the main groups of cardiovascular deaths, related categories to which coronary or stroke deaths might be attributed (e.g. hypertensive disease or diabetes mellitus), other major causes of mortality (e.g. cancers and respiratory diseases), causes with shared aetiology (e.g. lung cancer as a marker of smoking-related disease), and poorly specified causes such as ‘Signs, Symptoms and Ill-defined Conditions’ and ‘Sudden death, cause unknown’.

Comparison of routine mortality data and deaths classified according to the MONICA criteria are reported for coronary events by Tunstall-Pedoe et al. (3), and for stroke by Asplund et al. (4) on methods, and Thorvaldsen et al. (5) on results. Overall the results confirm the validity of the routine data for broad categories of deaths from stroke (ICD-9:430–438) (5). For coronary heart disease, deaths coded to ICD-8 or -9: 410–414 generally meet the MONICA criteria but mortality rates calculated from all deaths that meet the MONICA criteria were somewhat higher than rates based on the official statistics, with considerable variations between populations (3, 6). See also graphics G19 and G20.

Routine mortality data were used in testing the observed MONICA mortality and coronary-event rates, but are given special attention in this Monograph in Graphics G3–G6 and also in three MONICA Publications (7–9).

References
Annette Dobson

#17 Demographic Data

Use of population demographic data in MONICA

Data on the size of the study populations were one of the core data components of the WHO MONICA Project. They were used as the denominators for the calculation of coronary and stroke-event rates.

Requirements for the data

Demographic data had to be available for the same populations, defined by residence in the chosen administrative/geographic areas, in which the coronary and stroke registration, and the population surveys were carried out. The best routinely available mid-year estimates of the population were to be sent annually by the MONICA Collaborating Centres (MCCs) to the MONICA Data Centre (MDC). These were to be broken down by sex and 5-year age group for the 25–64 years age range, and optionally for the 65–74 age group (1).

Altogether, data were collected for 79 population units during 1980–1997. The period for different populations ranged from 7 to 16 years.

Sources of the data

The two main sources of the data were:

- computerized population registers, which usually provided reliable and accurate population figures, and
- systems based on decennial or other censuses with annual intercensal estimates, the quality of which depended on many factors.

The intercensal estimates were often provided by the national or regional authorities. In some cases, the population figures were available for census years only, and the intercensal estimates were produced by local agencies, the MCC or the MDC.

Quality of the data

Although bias (errors) in estimating populations sizes result in proportionately the same bias in calculating event rates, the quality of demographic data is seldom questioned in epidemiological studies. MONICA, however, applied strict quality control to the data:

- the data, which were received in the MDC on paper forms, were keyed. Checking for data-entry errors was done by scanning sums of rows and columns of the forms
- description of the details of local sources of data and the procedures used to process the data were obtained in collaboration with the MCCs
a special method was developed to check the internal consistency of the data for all reported years for each population.

These quality control procedures revealed major problems in the data for some populations. Some of the problems were due to inadequate intercensal estimation, and many of the problems could be remedied. Where intercensal estimation was based on census data only, the estimates were often accurate only for 2–3 years after the last census year. In two countries the official statistics were corrected after feed-back from the MONICA Project. More details about the demographic data and their quality control can be found in the MONICA Quality assessment report (2).

References
MONICA Web Publications are also accessible on the Monograph CD-ROM

Vladislav Moltchanov

#18 Health Services

With the realization that rapidly changing management of acute and sub-acute coronary heart disease could affect both the short and longer-term outcome of coronary events and possibly their frequency, MONICA Principal Investigators resolved in 1988 to collect additional data about the health services available for coronary heart disease in addition to the coronary care recorded in specific events, see #24 Acute Coronary Care.

Qualitative information relating to access to a range of services, diagnostic procedures and treatments was collected for the period 1980–92 from virtually all Reporting Units. The data collected included information on access to the following (see MONICA Manual Form UA (1)):

- emergency departments, ambulance services, cardiac surgery, cardiology
- echocardiography, coronary angiography, radionuclide imaging
- coronary artery bypass grafts (CABG), percutaneous transluminal coronary angioplasty (PTCA), thrombolytic drugs.

Evidence of the progressive improvement in the coverage of MONICA populations by ambulances with cardiac defibrillators and staff trained in their use, is one example of the findings to emerge from these data.

Further information on hospital utilization for coronary heart disease, and for coronary artery revascularization procedures (CARPs, that is coronary artery bypass grafts—CABG, and percutaneous transluminal coronary angioplasty—PTCA) was collected from MCCs with access to appropriate administrative statistical systems or procedure registers. Fifteen centres provided usable data but with varying periods of coverage. The data demonstrated large differences between populations in the rate of previous and new CARPs, not
explained by variations in coronary-event rates, and more likely to reflect availability of resources available in different healthcare systems. See MONICA Manual Forms UB (Hospital Separations), UC (Hospital Aggregate Bed Days), UD (Procedure Reporting Form) (1).

The Health Services component of MONICA was designated a core item and therefore the subject of the fourth MONICA Quality Control Centre, see #8 MONICA Quality Control Centres (MQCs). This occurred late on in MONICA. Some MCCs were unable to comply. In addition, the population denominators for these administrative data were often different from those that the MCCs used as Reporting Units or Reporting Unit Aggregates (RUAs) for their other analyses. The data were not used in testing either of the main hypotheses. Results have figured in MONICA internal presentations and in conference abstracts but there are, as yet, neither Data Books nor formal publications.

Reference
MONICA Web Publications are also available on the Monograph CD-ROM

Michael Hobbs

#19 Other Documents Used in MONICA

Introduction
Preceding sections described paper records, containing statistical data for their populations, sent in by MONICA Collaborating Centres (MCCs) for each calendar year. The exchange of paper and electronic records on MONICA data between the MONICA Data Centre and the MCCs is described in #36 Data Transfer, Checking and Management and in detail in the MONICA Manual (1), including the inventories and communication logs designed to prevent errors. The purpose of this section is to describe documents not featuring in the MONICA Manual. MONICA Memos are described in #11 Communications in MONICA, listed in #88 MONICA Memos, and are reproduced in the second CD-ROM They make a chronological list of MONICA’s preoccupations as it developed, including most of the documents described below. In each case the first relevant Memo is listed, not the later ones.

Annual Progress Reports (MONICA Memo 12, 6 June 1983)
MCCs were required to send annual progress reports to the MONICA Management Centre (MMC). Other MONICA centres, MQCs and MDC were required to provide six-monthly reports. These were a source of information about what was, and was not happening in different centres, and of any problems the Principal Investigator wished to report. Early sets of progress reports were circulated as MONICA Memos. Later MONICA concentrated on the timely delivery, quality and completeness of data reaching the MONICA Data Centre, a more fundamental indicator of what was happening. So progress reports figured less prominently.
MONICA Local Manuals  
(MONICA Memo 15, 12 August 1983)

At the start, candidate MCCs were required to provide their locally written Manual of Operations and Record Forms, translated into English where necessary, showing that they had conducted pilot studies, particularly on coronary-event registration, and would conform with the MONICA Protocol. These were to be approved by two members of the MONICA Steering Committee, see #10 Recruitment of Populations. This exercise had its limitations. Manuals were heavy documents, difficult to move round the world, and tedious to review. Investigators could readily duplicate parts of the existing MONICA protocol and manual of operations. Reviewers found it easier to detect definite errors than omissions in the text. Descriptions of pilot studies were sometimes cursory. Later, when some MCCs were failing, the question arose as to whether this exercise could have been done better. The task of reviewing 30 or more manuals had been formidable.

Local record form formats and questionnaires continued to be collected for the Data Centre as these were revised.

Sample Case-Histories for Test-Coding  
(MONICA Memo 18, 4 October 1983),  
ECGs for Coding with MONICA Criteria  
(MONICA Memo 31, 21 May 1985)

Testing and training material from two of the MQCs could be sent on paper as MONICA Memos to the MCCs who sent their codings back to the MQC. The MQCs returned to them their individual scores and remarks and an overall assessment and commentary would appear later in a further MONICA Memo. This was an iterative process that created further training and testing material with standard answers, and accounted for many of the early MONICA Memos. In a similar manner, quality control specimens were distributed to participating laboratories for lipid (and early-on for thiocyanate) analysis.

Sample Selection Description  
(MONICA Memo 50, 6 July 1985)

Although many MCCs used simple random sampling for their population surveys, this was not true of all of them. Information in the MONICA Data Centre on what sampling procedures and what sampling frames were being used was inadequate. This and Memo 68 addressed these issues, see #28 Sampling.

Annual Hospital Enzyme Use Reporting Form  
(MONICA Memo 56, 16 August 1985)

MONICA devoted considerable effort to the standardization of the coding of electrocardiograms, see #22 Minnesota Coding of the Electrocardiogram, but cardiac enzyme results were potentially more important in the diagnosis of definite myocardial infarction, see #23 Diagnosing Myocardial Infarction and Coronary Death. MONICA investigators had no control over which enzyme tests were done in their local hospitals, in their standardization, or in changes of these over time—a possible source of both between-population bias, and of spurious trends over time within populations. This Memo and form were an attempt to record what was happening in each local hospital, in terms of which tests were used and their designated normal values. It addressed an important issue but was abandoned except as a local option. The information was potentially valuable within each MCC, but not helpful to the MONICA Data Centre, as the central pooling record for coronary event did not record which hospital, enzymes or isoenzymes were involved in a particular case.
**Site Visit Procedures**  
(MONICA Memo 68, 20 March 1986)

Originally, review of Manuals was to be supplemented by site visits. These were costly in time and other resources, so original plans to visit every centre proved impracticable. Many of the site visits that did take place were precipitated by serious problems or were opportunistic with the visitor calling in at the local MONICA centre when travelling nearby for another reason. There was a difficult balance between critically reviewing the procedures of a multifaceted study on site, encouraging the local team, and meeting civic dignitaries and leading medical people to reinforce the team and its need for support and resources.

Event registration was continuous, but population surveys were intermittent, so what could be reviewed varied according to timing. Finally, site visitors needed to be fully briefed beforehand. After initial experiences it was decided to design a detailed questionnaire for MCCs which covered all the questions that should figure in a site visit. Results of this proved invaluable. While designed as a preliminary for site visits, it indicated whether or not they might be necessary.

**Coronary and Stroke Event Registration Procedures**  
(MONICA Memo 117, 17 December 1987)


After the MDC had started collecting data, it became apparent that information on the local manuals and site visit forms was still insufficient to enable proper assessment of the quality of the data coming from different MCCs. Detailed questionnaires on coronary and stroke event registration procedures (sent as a Memo) as well as on population survey procedures (sent directly to MCCs by the MDC) were prepared centrally and then completed by each MCC. The first survey procedure questionnaire in 1991 was used to document procedures in the completed initial and middle surveys, and what was planned for remaining surveys. In the second round in 1995, information on the now completed middle and final surveys was corrected or confirmed.

Together with the site visit forms, the procedure questionnaires provided information that was unavailable elsewhere and was used by different Quality Assessment groups (2).

**References**

MONICA Web Publications are also available on the Monograph CD-ROM


**Hugh Tunstall-Pedoe**