

MONICA Optional Studies

#43 Optional Studies—Beyond the Core

See #9 MONICA Reference Centres (MRCs) for further information

Core versus optional

When MONICA was launched it had the ambitious objective ‘to assess the extent to which trends in cardiovascular disease . . . are related to changes in known risk factors, daily living habits, health care, or major socioeconomic features . . .’ It then qualified this with ‘Collaborating centres will wish to cover all these areas, but the basic protocol covers key items only, leaving the rest as local options’. This ambitious manifesto, tempered by alarm as to what it might involve, and rapid compromise, demonstrates the dilemma posed by MONICA. Key items, subsequently labelled core items, were fundamental to the MONICA hypotheses. For these, there were standard protocols and methods of measurement that were usable by all participating centres. There were other factors for which standard, cross-cultural protocols and procedures were not available, or would be too expensive for general use. Collecting core data items for ten years or so was a formidable challenge, even without adding others. However, if we stopped at core items, there was a risk that the study would be criticized for being traditional and boring. It would lack spice and excitement if others were not added. Yet adding in costly, unproven and non-standardized factors would detract from the core, perhaps even affecting its quality, and would inhibit widespread participation. (1)

Interchange between core and optional

Local investigators were free to add additional questions or data items to their registration or population survey records. ‘Local options’ were of no concern to the MONICA Project as such, so that it was core items alone that were forwarded to the Data Centre in Helsinki. However, some items considered ‘optional’ at the start were subsequently added late as ‘core items’ to the registration and survey record forms, in particular questions relating to new coronary care drugs, additional questions on smoking and passive smoking, but also waist and hip circumference. There was also a tendency to go the other way if there were problems. This was true of serum thiocyanate and HDL-cholesterol, neither of which was fundamental to the MONICA hypotheses, nor actually core items, but for which protocols, procedures and data formats were specified at the start. Subsequent analysis of the data (thiocyanate), and quality control performance (HDL-cholesterol) showed that results should not be used for cross-sectional and longitudinal trends within MONICA centres as a whole, although they were potentially usable locally (2–4). Although psychosocial studies were generally considered optional, data items on marital and educational status were ‘core’, and analysed as such in a MONICA Quality assessment report (5).

Problems of collaboration in optional studies

Where there was sufficient interest in a particular option, MONICA investigators were encouraged to develop common methods and data sets for voluntary

- interchange between core and optional items
- interchange between local options and collaborative options
- MONICA ‘add-on’ studies have done much good work



Blood contains more than cholesterol

collaboration within MONICA. This applied particularly to some areas considered fundamental to coronary disease—diet, exercise and psychosocial factors. Launched later than the core study, and usually unable therefore to generate anything more than cross-sectional data, the MONICA optional studies were not given the attention or resources of core items, unless external funding was found. It needed an enthusiastic well-resourced coordinator to make an optional study succeed. Coordinators of topics such as drugs, diet, and physical activity changed at least once during MONICA, whereas psychosocial studies were subdivided.

Publication lists from individual populations record the variety of local options that were added by individual investigators, as will a bibliographic search of the literature for the newer risk factors. Some investigators published independent studies of risk factors (for example diet, vitamins) that colleagues elsewhere pursued in MONICA collaborative optional studies. Some centres concentrated on the core protocol. Some gave this less attention than other items that could be added in, particularly to population surveys. Many optional studies involved interdisciplinary and interdepartmental collaborations. The number of publications arising from multi-centre collaboration in optional studies is small compared with the number of single centre publications in the same areas. Heavy commitment of time, resources and funding to the core study, lack of involvement of the MONICA Data Centre, lack of time at Principal Investigators Meetings, all made the MONICA collaborative optional studies the Cinderella of MONICA. Yet paradoxically, MONICA investigators, usually using the MONICA framework, are major contributors to the literature on newer non-classic risk factors.

The following sections, #44–#49, are devoted to brief accounts of some of the MONICA optional studies. Individual investigators describe their local options in their own population pages and among their publications, or on their websites. See #51–#83.

References

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

1. WHO MONICA Project. MONICA Manual. (1998–1999). Part I: Description and Organization of the Project. Section 1: Objectives and Outline Protocol. Available from URL: <http://www.ktl.fi/publications/monica/manual/part1/I-1.htm>, URN:NBN:fi-fe19981147. MONICA Web Publication 1.
2. WHO MONICA Project. MONICA Manual. (1998–1999). Part III: Population Survey. Section 2: Standardization of lipid measurements. Available from URL: <http://www.ktl.fi/publications/monica/manual/part3/iii-2.htm>, URN:NBN:fi-fe19981152. MONICA Web Publication 1.
3. WHO MONICA Project. MONICA Manual. (1998–1999). Part III: Population Survey. Section 3: Standardization of thiocyanate measurements. Available from URL: <http://www.ktl.fi/publications/monica/manual/part3/iii-3.htm>, URN:NBN:fi-fe19981153. MONICA Web Publication 1.
4. Marques-Vidal P, Ferrario M, Kuulasmaa K, Grafnetter D, Moltchanov V, for the WHO MONICA Project. Quality assessment of data on HDL cholesterol in the WHO MONICA Project. (June 1999). Available from URL: <http://www.ktl.fi/publications/monica/hdl/hdlqa.htm>, URN:NBN:fi-fe19991137. MONICA Web Publication 11.
5. Molarius A, Kuulasmaa K, Moltchanov V, Ferrario M, for the WHO MONICA Project. Quality assessment of data on marital status and educational achievement in the WHO MONICA Project. (December 1998). Available from URL: <http://www.ktl.fi/publications/monica/educ/educqa.htm>, URN:NBN:fi-fe19991078. MONICA Web Publication 14.

Hugh Tunstall-Pedoe

#44 MONICA Optional Study on Nutrition

See #9 MONICA Reference Centres (MRCs) for further information

The collection of dietary data was optional in the MONICA project. Between 1982 and 1985 several meetings were held to discuss what dietary survey method should be used (1). The three-day record was selected as the preferred method. Between 1982 and 1989 dietary survey data were collected using either three or seven-day records in nine European MONICA centres. This survey was later carried out between 1994 and 1996 by seven centres. In total about 7000 men aged 45–64 participated in the different surveys. Guy de Backer, University of Ghent, Belgium coordinated the optional study on nutrition until 1994. In 1995 that responsibility was transferred to Daan Kromhout, RIVM, Bilthoven, The Netherlands.

The aim of the dietary surveys was to study trends in diet in relation to trends in cardiovascular (CVD) morbidity and mortality. Complete data are available from only six centres. It is therefore not possible to study associations between trends in diet and trends in CVD morbidity and mortality at the population level. The available data will be used to describe changes in dietary pattern during a 10-year period and to study prospectively diet-CVD relationships in about 5000 men aged 45–64 at baseline and followed up for CVD morbidity and mortality since 1982–1989. The dietary record data collected in the Caerphilly Study in the period 1979–1983 were added to the data collected by the nine MONICA centres surveyed in that period. The emphasis in data analysis will be on fish and plant foods and on fatty acids and antioxidants in relation to CVD occurrence.

In the period 1995–1999 an inventory was made about the way dietary data were collected, coded and transformed from foods to nutrients in the different MONICA centres. A database was prepared that presented dietary data in a standardized way. In addition, two grant proposals were prepared for the European Union, one in the context of the FAIR Programme and another one for the 5th Framework Programme. Neither proposal was funded. Two nutritional epidemiologists worked on the database in the period 1995–1999. A post-doctoral researcher worked on preparation of the database during 2002. Thereafter data analysis can start.

Reference

Haveman-Nies A, Bokje E, Ocké M, Kromhout D. MONICA Optional Study on Nutrition: the dietary assessment methodology. RIVM report 261753001/2002. Available from URL: <http://www.rivm.nl/bibliotheek/rapporten/261753001.pdf>.

Daan Kromhout

#45 MONICA Optional Study on Antioxidant Vitamins and Polyunsaturated Fatty Acids (PUFA)

See #9 MONICA Reference Centres (MRCs) for further information

The vitamin-antioxidant hypothesis became the subject of intense interest shortly after MONICA was launched. One of the champions of this hypothesis was Fred Gey who lobbied for MONICA participation in a study organized from his base in the laboratory of a Swiss drug company (Hoffmann-La Roche). This company provided funding for recruitment of subjects, specimen collection, storage and transfer of specimens, laboratory assay and data analysis. This

- nutritional intake is difficult and expensive to measure
- national and cultural differences make standardized measurements difficult to achieve



People change what they eat

- the vitamin-antioxidant hypothesis became prominent during MONICA
- centrally funded, this study produced results and publications



Fred Gey promoted the vitamin-antioxidant hypothesis



How do fruit and vegetables help the heart?

substudy produced results and publications (1, 2). Coordination of vitamin studies was transferred to the University of Bern when Fred Gey moved there. On his retirement from there it was transferred to the Belfast Centre for work on other analytes from the original specimens.

References

1. Gey KF, Stahelin HB, Puska P, Evans AE. Relationship of plasma level of vitamin C to mortality from ischemic heart disease. *Annals of the New York Academy of Sciences*, 1987, 498:110–123. PMID: 3497600.
2. Gey KF, Puska P. Plasma vitamins E and A inversely correlated to mortality from ischaemic heart disease in cross-cultural epidemiology. *Annals of the New York Academy of Sciences*, 1989, 570:268–282. PMID: 2629597.

Hugh Tunstall-Pedoe

#46 MONICA Optional Psychosocial Substudy (MOPSY)

See #9 MONICA Reference Centres (MRCs) for further information

Aims

The aims of the MONICA Psychosocial study were:

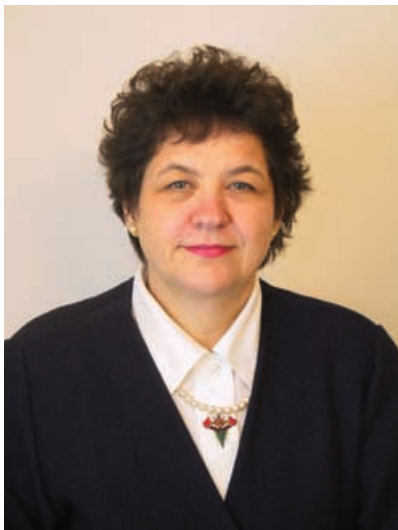
- coordinated from the European Office of WHO
- produced hypotheses, protocols and local publications
- problems of standardization of questionnaires

- to clarify the relationship between 10-year trends in certain psychosocial factors and corresponding trends in the incidence of cardiovascular disease, in order to provide estimates of the relative importance of psychosocial risk factors and standard risk factors in predicting and controlling cardiovascular disease in populations
- to foster cooperation for the development of a battery of standardized, internationally comparable methods for the assessment of psychosocial factors related to health.

Psychosocial variables under study

In addition to the core MONICA data, the centres participating in the MONICA Psychosocial Study were also obtaining information for the defined populations under study on the following psychosocial variables:

- type A coronary-prone behaviour pattern
- health knowledge and attitudes
- work characteristics
- life stress (life events)
- vital exhaustion and sleep disturbances
- other psychological variables
- social support
- socioeconomic characteristics on an aggregated level
- social and geographical mobility.



Aushra Shatchkute

Hypotheses to be tested

The central null hypotheses to be tested were parallel to those of the core MONICA project:

1. For the participating centres there is no relationship between changes in psychosocial risk factors and changes in the incidence of coronary heart disease (CHD) (fatal plus non-fatal cases) over a 10-year period.

2. For the participating centres there is no relationship between changes in psychosocial risk factors and changes in the incidence of classical coronary risk factors.

Within the MONICA centres the following general hypotheses were proposed for testing:

1. Different levels of psychosocial risk factors in individuals are not related to differences in the prevalence of CHD morbidity (for example measured by ECG, angina pectoris questionnaire). To be tested in the cross-sectional studies.
2. Different levels of psychosocial risk factors in individuals are not related to different risks of CHD mortality and morbidity. To be tested in cross-sectional and cohort studies.
3. Different levels of psychosocial risk factors are not related to prevalence and incidence of the classical coronary risk factors. To be tested in cross-sectional and cohort studies.

A Data Management Centre was established at the MEDIS Institute in Munich, Germany (Institut für Medizinische Informatik und Systemforschung). Nineteen centres sent data for central processing at the Centre.

However, international comparability has been limited through the lack of standardized questionnaires. Therefore, for the second and third surveys, a manual of operations with recommendations for standardized measurements was introduced.

The main achievements of the MONICA Psychosocial Substudy were the establishment of an international network to study CVD psychosocial risk factors, and the elaboration of standardized questionnaires to assess these factors. This group of studies produced considerable discussion, and some common questionnaires, but most activity in this area seems to have been at a local rather than at a multi-centre collaborative level. Many MCCs have published data on social deprivation and its relation to risk factors and cardiovascular disease.

Aushra Shatchkute

#47 MONICA Optional Study of Physical Activity (MOSPA)

[See #9 MONICA Reference Centres \(MRCs\) for further information](#)

The reference centre for physical activity was initially in Tel Aviv, but this group encountered problems with implementing the core protocol. The enthusiasm of the CDC Atlanta group for their developing questionnaire, and offer of free data analyses, at the Council of Principal Investigators Meeting in Lugano in 1990, led many MCCs to incorporate it as an 'add-on' to their middle and/or final MONICA population surveys.

The WHO MONICA Optional Study of Physical Activity (MOSPA) questionnaire was developed by the Centers for Disease Control and Prevention (CDC) with the assistance of several experts and individuals involved with the WHO MONICA Project. The instrument was put into its final form on 4 December 1987 and distributed in MONICA MEMO 115 (see #88 *MONICA Memos* and the MONICA CD-ROM). The MOSPA questionnaire is divided up into four activity categories or domains. Physical activity questions cover occupational, travel to work, household, and leisure-time physical activity.

- physical activity is easy to recognise but not so easy to measure
- a standard questionnaire was eventually used by several MONICA centres
- introduced too late for the study of 10-year trends



Cycling—USA



Cross-country skiing—Finland

Since it was included among the Collection of Physical Activity Questionnaires for Health-Related Research (1) we continue to receive requests for the questionnaire and supporting documentation.

As the MOSPA Data Management Centre, the CDC (Atlanta, USA) developed the MOSPA algorithm, edited and analysed data sets from MOSPA participating sites, and submitted a comprehensive physical activity report to each MOSPA site. In 1997, the following MOSPA sites received analyses of minutes/week and MET (metabolic equivalent task) minutes/week for light, moderate, vigorous and overall intensity levels for each physical activity domain: MOSPA-Augsburg, MOSPA-Catalonia, MOSPA-East Germany, MOSPA-Friuli, Pol-MOSPA-Krakow, Pol-MOSPA-Warsaw, Scottish MOSPA, Sino-MOSPA Beijing, and Siberian MOSPA.

Reference

1. Pereira MA, FitzerGerald SJ, Gregg EW, Joswiak ML, Ryan WJ, Suminski RR, Utter AC, Zmuda JM. A collection of Physical Activity Questionnaires for health-related research. *Medicine and Science in Sports and Exercise*, 1997, 29(6Suppl):S1–S205. PMID 9243481. (the CDC questionnaire is on pages S162–S169).

Deborah Jones

#48 MONICA Optional Study on Drugs

See #9 MONICA Reference Centres (MRCs) for further information
Earlier activity in this area was carried out in Oslo

- MONICA concluded at its end that drug usage influences cardiovascular disease
- yet it failed to plan measurements of drug use in the population as a core item
- hence the MONICA Optional Study on Drugs

Although drugs are of major medical, social and economic importance in the context of cardiovascular disease, the MONICA core study included only minimum information about drug utilization. Several PIs, however, considered this topic important enough to acquire more detailed information beyond the core during the MONICA population surveys, using their own methods, but within the framework of the MONICA Optional Study on Drugs. The Bremen Institute for Prevention Research and Social Medicine (BIPS) was appointed the Reference Centre for Drug Epidemiology (MRC-Drugs) for this optional study because of its previous activities and experience in this field. The MRC-Drugs asked each MCC about drug data acquisition and availability for the joint analysis, which started in 1997 and was based on survey data from 26 regional surveys from 12 MCCs in seven countries. This made a total of 39 260 survey participants, aged 35–64 years. The first results of investigations into antihypertensive drug treatment and its relation to hypertension control and myocardial infarction have recently been published (1). Further analyses are planned. Among others, these analyses will focus on specific antihypertensive drug groups and on serum lipid-reducing drug treatment.

Reference

- Janhsen K. *Joint Analysis of the MONICA Optional Study on Drugs: Antihypertensive Drug Treatment in an International Comparison and its Relations to Hypertension Control and Myocardial Infarction*. [Doctoral dissertation]. Bremen, University of Bremen, 2001.

Eberhard Greiser, Katrin Janhsen



#49 MONICA Optional Study on Haemostatic Risk Factors

See #9 MONICA Reference Centres (MRCs) for further information

This study was funded by the British Heart Foundation. During the final MONICA population survey (1991–1997), samples were collected, using a standardized protocol, from men and women aged 45–64 years in 12 populations, eleven of them European. Laboratory analyses took place in Bristol and in Glasgow. Results were available for 3250 subjects (Bristol samples) and 2372 subjects (Glasgow samples). Mean population levels of haemostatic risk factors were adjusted for age, smoking habit and body mass index. In general, populations with a high incidence of CHD had higher levels of haemostatic risk factors. Correlations between coronary-event rates current at the time of the surveys and population levels of haemostatic factors were significant in the case of the vWf antigen for men and women ($r = 0.69$ and 0.88) and for nephelometric fibrinogen ($r = 0.78$) for men and D-dimer ($r = 0.84$) for women.

C reactive protein is being measured in the populations; DNA has been collected and may be used to genotype risk factors of interest. Results are being prepared for formal publication.

References

1. Yarnell J, McCrum E, Evans A, Rumley A, Lowe G. Haemostatic cardiovascular risk factors in the WHO MONICA Project: an international comparison. *Blood Coagulation and Fibrinolysis*, 1999, 10:No.8, 015(Abs). (PMID: nil).
2. Yarnell JWG, Sweetnam PM, Rumley A, Lowe GDO. Lifestyle and hemostatic risk factors for ischemic heart disease. The Caerphilly Study. *Arteriosclerosis Thrombosis and Vascular Biology*, 2000, 20:271–279. PMID: 10634829.

John Yarnell, Evelyn McCrum, Alun Evans

- association between population levels of CHD and von Willebrand's factor



