WHO MONICA Project and its Connections to the North Karelia Project

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ABSTRACT

The World Health Organization's MONICA (Multinational Monitoring of Trends and Determinants in Cardiovascular Disease) Project was established after the increase in mortality from coronary heart disease had turned to a decline in some countries. Its objective was to measure the trends in cardiovascular mortality and coronary heart disease and cerebrovascular disease morbidity, and to assess the extent to which these trends were related to changes in known risk factors and health care measured at the same time in defined populations in different countries. Thirty-one centers in 21 countries carried out the monitoring over a period of 10 years in the 1980s and 1990s. The project provided information on disease rates, risk factors, and treatment for the first time in most of the study populations. The results answered some of the initial questions and opened new questions on the complexity of the associations between disease trends and their determinants. MONICA had a major impact in training cardiovascular epidemiologists and in creating measurement standards for international use.

In all the countries where the national statistics were available, mortality from coronary heart disease was increasing. In the 1970s it was observed that coronary heart disease mortality had turned to a decline in the 1960s in the United States, Canada, and Australia. The U.S. National Heart, Lung, and Blood Institute organized a conference on this change in the trend in 1978 [1]. One of the questions raised was whether the statistics reflected real changes in the population or were confounded by changes in coding practices—a large proportion of those dying, possibly from a heart attack, die without a medical presence, and little information is available for the diagnosis. If the changes were real, how were they related to changes in medical care and changes in risk factors? To address these questions, the World Health Organization (WHO) coordinated the planning of the MONICA (Multinational Monitoring of Trends and Determinants in Cardiovascular Disease) study [2]. The basic idea was to monitor trends in coronary heart disease and stroke mortality and morbidity, trends in known risk factors, and trends in acute coronary care in several geographically defined populations in different countries over a period of ten years, and then to assess the relationships between these trends.

STUDY DESIGN

In each defined population during a 10-year period, annual data on population size and numbers of death from selected causes were collected from routine administrative statistics. Registration of acute coronary events, diagnosed using strict study criteria was organized, or optionally, registration of stroke events was organized. Two risk factor

surveys, 1 in the beginning and 1 at the end of the 10-year period, and optionally a third one in between, were organized in independent population samples. The details of acute coronary care were to be collected for 500 consecutive cases of the coronary events registration toward the beginning and at the end of the 10-year period. This included recording of medication and other medical procedures before, during, and after the acute event [2,3].

At that time, there was already plenty of evidence about smoking, blood pressure, and blood cholesterol being major risk factors. The potentially wider role of nutrition and physical activity were acknowledged, but collection of data on these was considered too difficult to standardize cross the populations. However, these were considered in optional studies among some of the MONICA centers. Other optional studies were organized on antioxidant vitamins and polyunsaturated fatty acids, psychosocial factors, drugs, and hemostatic risk factors [2].

There was no follow-up of persons in MONICA except for 28 days for the coronary and stroke events to assess their fatality. It was an ecological study relating the associations between risk factors, treatment, and disease at a population level, rather than in individuals.

STUDY POPULATIONS AND ORGANIZATION

Data collection in the study populations was organized by the MONICA Collaborating Centres (MCC). Any center could join the study with 1 or several populations provided that it was able to collect the data as specified in the MONICA manual and it was able to fund the data collection. Forty MCC from 26 countries started the study and 31 MCC from 21 countries completed 10-years of data

collection. These provided 38 populations for the final analyses (Figure 1).

The coordinating center activities were shared between WHO headquarters in Geneva, which hosted the MONICA management center, and the National Public Health Institute of Finland, which hosted the MONICA data center. MONICA paid particular attention to attaining a high quality of data. In addition to the work at the data center, separate external quality control centers to supplement and complement the internal quality control work

FIGURE 1. MONICA Populations. MONICA, Multinational Monitoring of Trends and Determinants in Cardiovascular Disease. Reproduced from MONICA Monograph [2].

within each MCC were located in Prague, Czechoslovakia (later Czech Republic) for lipid measurements; Budapest, Hungary, for electrocardiogram coding; Dundee, Scotland, for event registration; and Perth, Australia, for data on health services.

RELATIONSHIP BETWEEN MONICA AND THE NORTH KARELIA PROJECT

The provinces of North Karelia and of Kuopio and the city of Turku together with a nearby rural area in southwest Finland participated in the MONICA project in the years 1982 to 1992 under the name FINMONICA. In North Karelia and Kuopio Province, this was a continuation of the North Karelia Project risk factor surveys. Coronary event registration started in North Karelia in 1972. Because of the experience gained in the North Karelia Project and the desire to expand international collaboration, the North Karelia investigators were closely involved in the planning of the MONICA Project. Pekka Puska was one of the first elected members of the MONICA Steering Committee.

After negotiations with several countries, it was agreed to locate the MONICA data center in the National Public Health Institute of Finland, which also coordinated the North Karelia Project. To our knowledge, this choice was supported not only by the North Karelia experience but also by Finland's geopolitical position at the time of the cold war. It was considered important to keep the MONICA data center operationally independent of FINMONICA, which formally had the same relationship as any other MONICA collaborating center with the MONICA data center. Nevertheless, FINMONICA and the North Kareli project provided a near-by window for the MONICA data center to see and understand the activities of a MONICA collaborating center.

MAIN FINDINGS AND IMPLICATIONS OF MONICA

MONICA confirmed that the large variations between countries in the levels and trends of coronary heart disease and stroke mortality were real [4–6]. Where coronary heart disease mortality was declining, two-thirds of the decline was due to the decline in event rates and one-third was due to the decline in case fatality (Figure 2) [2,5].

MONICA also showed, for the first time, comparable estimates of risk factor levels and trends for a large number of populations in different countries [2,7,8].
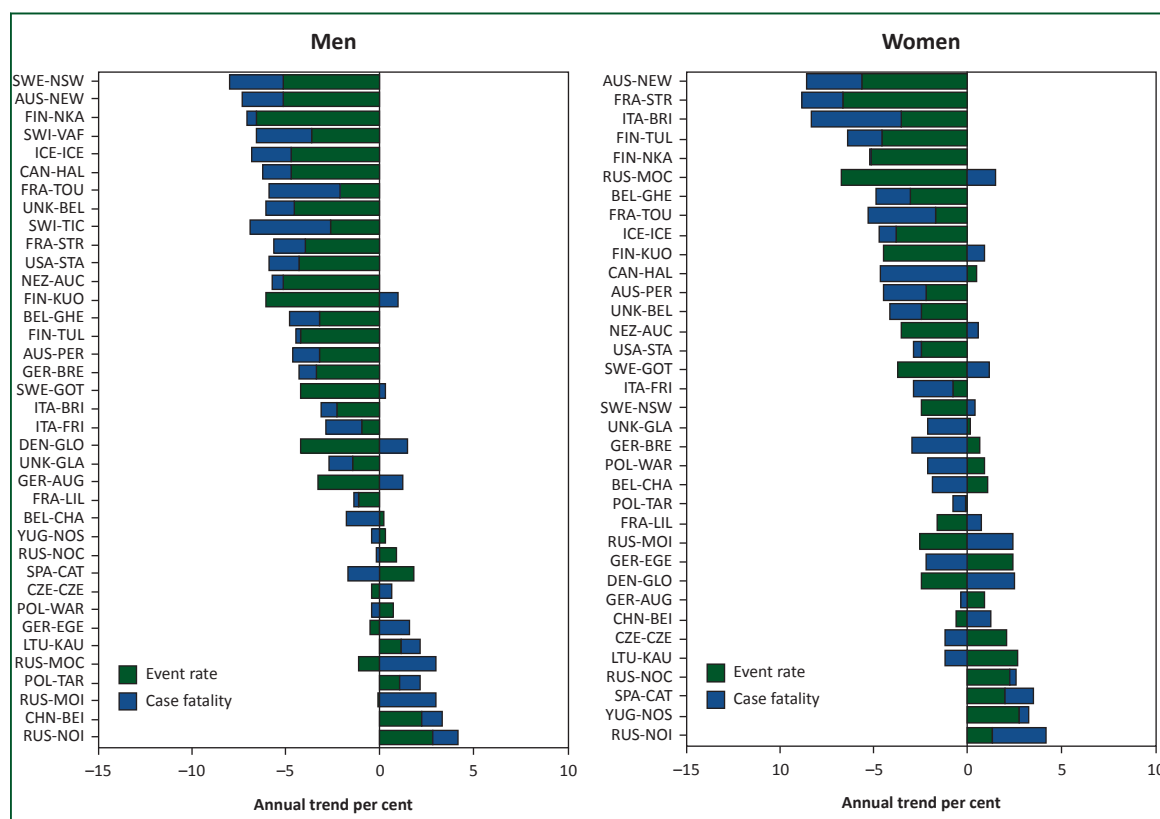

FIGURE 2. Average annual change in coronary heart diseases mortality (total bar) in individual MONICA populations, partitioned between the contribution from change in event rate (green bar) and that from change in case fatality (blue bar). MONICA, Multinational Monitoring of Trends and Determinants in Cardiovascular Disease. Reproduced from MONICA Monograph [2], adapted from Tunstall-Pedoe et al. [5].
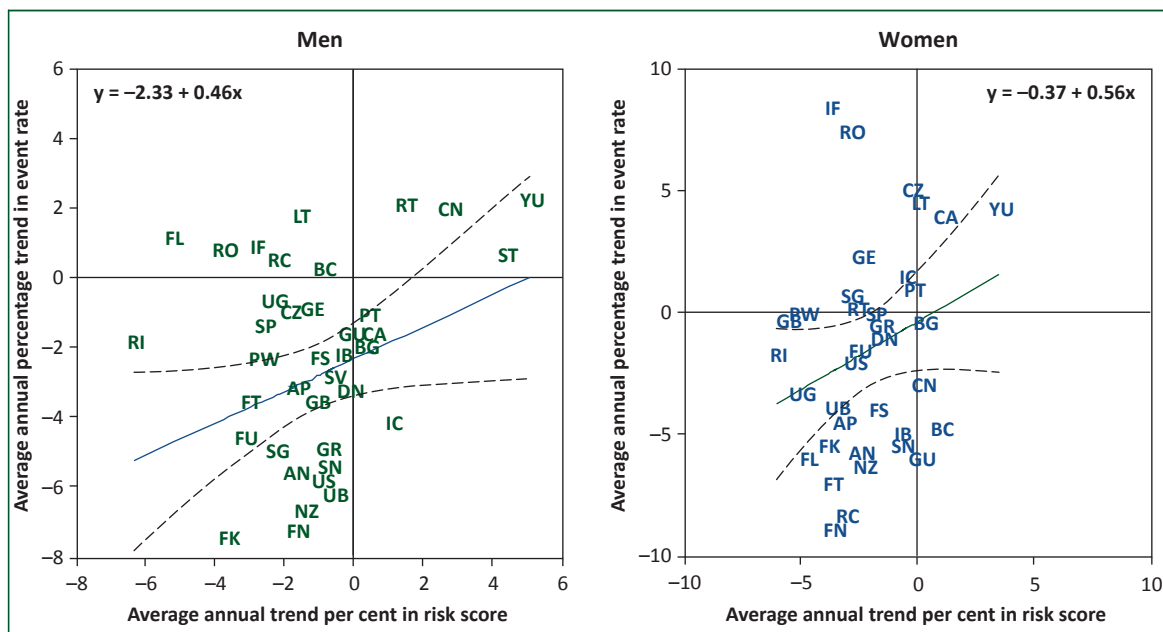
FIGURE 3. Change in coronary event rate versus change in risk score for lagged event rate period in the MONICA populations. The 5-year time lag used for the figure improved regression over that without; a greater time lag would have necessitated a longer registration period and more survey data points. MONICA, Multinational Monitoring of Trends and Determinants in Cardiovascular Disease. AN, AUS-NEW; AP, AUS-PER; BC, BEL-CHA; BG, BEL-GHE; CA, CAN-HAL; CN, CHN-BEI; CZ, CZE-CZE; DN, DEN-GLO; FK, FIN-KUO; FN, FIN-NKA; FU, FIN-TUL; FL, FRA-LIL; FS, FRA-STR; FT, FRA-TOU; GR, GER-AUG (rural); GU, GER-AUG (urban); GB, GER-BRE; GE, GER-EGE; IC, ICE-ICE; IB, ITA-BRI; IF, ITA-FRI; LT, LTU-KAU; NZ, NEZ-AUC; PT, POL-TAR; PW, POL-WAR; RC, RUS-MOS (control); RI, RUS-MOS (intervention); RO, RUS-NOV (control); RT, RUS-NOV (intervention); SP, SPA-CAT; SG, SWE-GOT; SN, SWE-NSW; ST, SWI-TIC; SV, SWI-VAF; UB, UNK-BEL; UG, UNK-GLA; US, USA-STA; YU, YUG-NOS. Reproduced from MONICA Monograph [2], adapted from Kuulasmaa et al. [9].

In the ecological analysis, about one-half of the variation of the trends in coronary event rates was explained by the risk factor trends (Figure 3) [9]. To what extent the rest of the variation in trends in event rates is explained by other factors and to what extent by longer term effects of the risk factors remains an open question. The Finnish populations in Figure 3 (FN = North Karelia, FK = Kuopio Province, and FT = Turku-Loimaa) each had a clear decline in their combined risk factor score and a particularly strong decline in event rates.

MONICA was lucky to monitor the introduction of many new treatments for coronary heart disease from the 1980s to 1990s: beta blockers; aspirin; thrombolytic therapy; angiotensin-converting enzyme inhibitors; and cardiac revascularization [2,10]. There was a strong negative correlation in the ecological analyses, across populations, between changes in the treatments on one side and case fatality on the other, and even stronger between change in the treatments and event rate or mortality, suggesting that coronary care and secondary prevention are strongly linked with the decline of coronary events. However, there was a strong east-west gradient in the changes, suggesting that the associations might be partly explained by other differences between countries with different economies [10].

Perhaps the biggest impact of MONICA relates to the facts that it facilitated reliable monitoring of the trends in cardiovascular diseases and their risk factors in a large number of countries and it helped to train cardiovascular epidemiologists in these countries. In the beginning, many of the countries had little experience in monitoring whole populations. However, there was interest in it, and MONICA gave the opportunity to learn together with others and to standardize local results to make them comparable between centers. Through MONICA and the related studies that it inspired, most of the research groups have had a key role in cardiovascular epidemiology and prevention both within their own countries and internationally; their successors are building on this.

What was also not so obvious at the beginning of MONICA, and even today, is the detailed documentation of not only the study procedures but also the successes and failures of the standardization of the disease and risk factor monitoring. When the project was approaching completion, the principal investigators of the collaborating centers unanimously agreed to publish these. This documentation was published in MONICA's web publication series [11], and summaries have been published in peer-reviewed journals.

LIFE AFTER MONICA

MONICA's main results were published by the early 2000s, and a monograph of the study was published in 2003 [2]. The joint dataset was archived in an easy to use format on CD-ROMs, which were made available to each collaborating center. After several years of active analysis and publication, the use of the data has decreased substantially in recent years. The data are getting outdated, but permissions to access the data for analysis remains complicated: approval is needed from each collaborating center whose data is to be used. However, the CD-ROMs attached to the MONICA monograph [2] include a 20% random sample of the individual level data, which can be used for pilot studies or for teaching.

Among MONICA's direct progeny are the MORGAM (MONICA Risk, Genetics, Archiving and Monograph) study and the EHES (European Health Examination Survey). When MONICA was coming to its end, it was found that many of the centers had followed up the cohorts examined in the risk factor surveys for death and cardiovascular events. Many of them had also collected DNA in the surveys and most still had frozen sera available. These cohorts initiated the MORGAM project to harmonize the follow-up data and some additional baseline data to form a large cohort covering different parts of Europe [12]. Also many other cohorts that had used MONICA-like procedures joined MORGAM. Today MORGAM has 27 participating centers from 15 countries with about 300,000 persons in the prospective cohorts [13]. These are being used to study various questions on the classic risk factors, genetics, and biomarkers, as well as their association with cardiovascular endpoints.

After MONICA, there was a lack of international standardization of risk factor surveys for major chronic diseases. In Europe, where an increasing number of countries organized national health examination surveys, the problem has been tackled in collaboration with the European Commission. In the EHRM (European Health Risk Monitoring) project, the MONICA survey manual was updated in 2002, 20 years after MONICA was started [14]. Little by little, this developed into EHES, whose objective was the standardization of the national health examination surveys in European countries [15]. In the past 6 years, national surveys standardized to EHES have been completed or are ongoing in 13 countries. The FINRISK surveys, which include the North Karelia Project, FINMONICA, and later five yearly surveys, are participating both in MORGAM and in EHES. Both of these collaborative activities are being coordinated by the National Institute for Health and Welfare of Finland, which is the successor to the National Public Health Institute.

REFERENCES

1. Havlik RJ, Feinleib M, editors. Proceedings of the Conference on the Decline in Coronary Heart Disease Mortality, 1978 Oct 24—25, Washington, DC. NIH Publication No. 79-1610 DHES. Bethesda, MD: National Heart, Lung and Blood Institute, 1979.
2. Tunstall-Pedoe H, editor. MONICA Monograph and Multimedia Sourcebook. Geneva: World Health Organization. Available at: http://www.who.int/iris/handle/10665/42597; 2003. Accessed December 5, 2015.
3. WHO MONICA Project: MONICA Manual. WHO MONICA Project e-publications [Internet]. 1998-1999; (1). URN:NBN:fi-fe19981146. Available at: http://www.thl.fi/publications/monica/manual/; March 31, 1999. Accessed December 5, 2015.
4. Tunstall-Pedoe H, Kuulasmaa K, Amouyel P, Arveiler D, Rajakangas AM, Pajak A. Myocardial infarction and coronary deaths in the World Health Organization MONICA Project: registration procedures, event rates, and case fatality in 38 populations from 21 countries in 4 continents. Circulation 1994;90:583–612.
5. Tunstall-Pedoe H, Kuulasmaa K, Mähönen M, Tolonen H, Ruokokoski E, Amouyel P. Contribution of trends in survival and coronary-event rates to changes in coronary heart disease mortality: 10-year results from 37 WHO MONICA project populations. Lancet 1999;353:1547–57.
6. Tolonen H, Mähönen M, Asplund K, et al., for the WHO MONICA project. Do trends in population levels of blood pressure and other cardiovascular risk factors explain trends in stroke event rates? Comparisons of 15 populations in 9 countries within the WHO MONICA Stroke Project. Stroke 2002;33:2367–75.
7. Pajak A, Kuulasmaa K, Tuomilehto J, for the WHO MONICA Project. Geographical variation in the major risk factors of coronary heart disease in men and women aged 35—64 years. World Health Stat Q 1988;41:115–40.
8. Evans A, Tolonen H, Hense HW, et al., for the WHO MONICA project. Trends in coronary risk factors in the WHO MONICA Project. Int J Epidemiol 2001;30(Suppl 1):S35–40.
9. Kuulasmaa K, Tunstall-Pedoe H, Dobson A, et al. Estimation of contribution of changes in classic risk factors to trends in coronary-event rates across the WHO MONICA Project populations. Lancet 2000;355:675–87.
10. Tunstall-Pedoe H, Vanuzzo D, Hobbs M, et al. Estimation of contribution of changes in coronary care to improving survival, event rates, and coronary heart disease mortality across the WHO MONICA Project populations. Lancet 2000;355:688–700.
11. WHO MONICA Project e-Publications. Available at: http://www.thl.fi/publications/monica/; January 4, 2013. Accessed December 5, 2015.
12. Evans A, Salomaa V, Kulathinal S, et al., for the MORGAM project. MORGAM (an international pooling of cardiovascular cohorts). Int J Epidemiol 2005;34:21–7.
13. The MORGAM Project. Available at: http://www.thl.fi/morgam/; April 18, 2015. Accessed December 5, 2015.
14. WWW-Publications from the European Health Risk Monitoring Project. Available at: http://www.thl.fi/publications/ehrm/; March 24, 2011. Accessed December 5, 2015.
15. European Health Examination Survey. Available at: http://www.ehes.info/; December 1, 2015. Accessed December 5, 2015.