## Risk factors: systolic blood pressure

Notes in italics are repeated to help random browsers—systematic readers should ignore them.

1. *The timing of the initial and final surveys differed by population. These surveys were usually eight to ten years apart but the interval could be as little as six years. The calendar years and months varied. See G10 and MONICA Quality assessment of age, date of examination and survey periods (1).*

2. Results are shown as the mean systolic blood pressure in millimetres of mercury, mmHg, for the 35–64 age group. *The results are age-standardized to minimize any effect of differing age structures on the apparent findings. See #38 Population Prevalence and Trends, #39 Age Standardization.*

3. *The graphs characterize men and women over a thirty-year age band in each survey for each population with a single value, but levels and trends vary with age. Age-specific data are published in the MONICA Data Book of population surveys, table 6.1.2 (1), and early results in MONICA Publication 11 (2).*

4. *Survey results could be influenced by failure to participate by some of those selected for the survey. The issue is complex. Different methods of recruitment and sampling were used in different populations. There is more than one definition of response rates. See#28 Sampling, #29 Recruitment and Response Rates, MONICA Quality assessment of participation rates, sampling frames and fractions (1).*

5. To convert to and from SI Units: 100 mmHg = 13.3 kilopascal (kPa); 10 kPa = 75 mmHg.

6. In a reading such as 156/82, the systolic blood pressure is the first, higher reading—156, and the second lower one—82, is the diastolic blood pressure. It was formerly believed that the diastolic blood pressure was of greater medical significance, and it was the target of medical intervention. Measurement of the systolic blood pressure is easier to standardize; it is now considered to be of equal or greater significance than diastolic blood pressure as a risk factor predicting cardiovascular disease; and it is increasingly the target of treatment. *See #32 Blood pressure.*

7. In the MONICA population surveys blood pressure was measured twice with the subject at rest, and the average of the two readings was used. See MONICA Manual Part III, Section 1 (1), MONICA Quality assessment of data on blood pressure (1).

8. Real differences in average blood pressure in populations over time and space are important to epidemiologists, but they could be spuriously created by bad measurement techniques. Readings are ephemeral and cannot be stored for re-measurement like blood specimens. Some centres used simple mercury sphygmomanometers and others more complex ‘random-zero’ mercury sphygmomanometers, designed to reduce observer bias. Extensive training, quality control and monitoring of performance were done to encourage standardized recording. See #32 Blood Pressure, MONICA Quality assessment of data on blood pressure (1). MONICA Publications 11, 14, 20, 31 (2).

9. The scale for men and women is the same, as is the range across populations of average systolic blood pressure. The latter varied by about 25 mmHg in the initial survey, and rather less in the final survey, where pressures appear more uniform. Rankings appear similar in the two sexes.

10. These graphs are based on the MONICA Data Book of population surveys, table 6.1.2 (1). The Data Book contains information on many more blood pressure items, such as diastolic blood pressure, blood pressure categories, and identification and treatment of hypertension in different populations. See MONICA Quality assessment of data on hypertension control (1), MONICA Data Book of population surveys, tables 6.1.2–6.1.6 (1).

11. The Data book also contains age-specific data (as did MONICA Publication 11) (2). These show that in many populations the blood pressure in women aged 35–44 is lower than that in men of the same age, but at 55–64 it is higher. The age-standardized readings shown here conceal this difference in age-gradients.

1. See Monograph CD-ROM or MONICA Website http://www.ktl.fi/monica/.
2. Full references and summaries of MONICA Publications appear in #85/86.
G40 Average systolic blood pressure in the initial risk-factor survey

Men

Women

G41 Average systolic blood pressure in the final risk-factor survey

Men

Women
Notes in italics are repeated to help random browsers—systematic readers should ignore them.

G42


2. The initial and final surveys did not take place exactly ten years apart, but this graph incorporates corrections to standardize the differences, as if they were being measured across ten years.

3. Horizontal bars in G42 show the 95% confidence intervals around the estimated 10-year trend. The smaller the length of the bars the more precise the estimated trend. If the bars fail to cross the zero line the estimated trend is considered to deviate significantly from zero. Declining trends are shown to the left of the zero line, increasing trends to the right.

4. Confidence intervals are similar for men and women; the population surveys sampled them in similar numbers.

5. To convert to and from SI Units: 100 mmHg = 13.3 kilo-Pascal (kPa); 10 kPa = 75 mmHg.

6. G42 shows similar trends in systolic blood pressure in men and women in the various populations. The majority of male populations show decreasing trends. Two-thirds of the populations show a decreasing trend, to the left of zero. The trend is increasing, to the right of zero in 12. In women, more populations show a decrease. Only seven have an estimated increasing trend. Age-specific data are available in the MONICA Data Book of population surveys (1).

G43

7. G43 is a spot map showing the geographical distribution of the results shown in G42. Many of the confidence intervals in G42 include zero, particularly in men. The populations concerned are marked with black spots. Those with a significant decrease in systolic blood pressure are shown with blue spots, while those with a significant increase are marked with red spots.

8. Only one population, Canada-Halifax, CAN-HAL, see #54, had a significant increase in mean systolic blood pressure in both men and women. It had the second lowest average systolic blood pressure in men in the initial population survey, and the lowest average in women. In the final survey CAN-HAL readings had increased but still remained low.

9. It is unlikely that blood pressure data of poor quality had a significant effect on overall MONICA results: G56 (see later) shows that most population RUAs had acceptable blood pressure quality scores and that these did not appear to relate strongly to trends in blood pressure. Ensuring continued high quality readings in the field is difficult however, and it is not possible to carry out external quality control or to archive material. Automatic machines may, in the future, remove some but not all, of the causes of variability and bias in blood pressure measurement. In the mid-1980s to mid-1990s they were not sufficiently tested and standardized for reliability and comparability to be recommended for the MONICA population surveys. Investigators were expected to replicate the same standard methods when repeating their population surveys.

10. See the MONICA Data Book of population surveys, tables 6.1.2–6.1.6 (1) for blood pressure items. MONICA Publications 14, 20, 31 (2) are on data quality and blood pressure levels, while MONICA Publication 11 (2) provided early cross-sectional data. For further information, see #32 Blood Pressure, MONICA Quality assessment of data on blood pressure (1), MONICA Quality assessment of data on hypertension control (1). Further publications will be listed on the MONICA Website (1) as they appear.

1. See Monograph CD-ROM or MONICA Website http://www.ktl.fi/monica/.
2. Full references and summaries of MONICA Publications appear in #85/86.
G42 Ten-year change in average systolic blood pressure

Men

Women

G43 Spot maps of population changes in average systolic blood pressure
**Risk factors: total blood cholesterol**

Notes in italics are repeated to help random browsers—systematic readers should ignore them.

1. **The timing of the initial and final surveys differed by population. These surveys were usually eight to ten years apart but the interval could be as little as six years. The calendar years and months varied. See G10 and MONICA Quality assessment of age, date of examination and survey periods.**

2. **Results are shown as the estimated mean total cholesterol in millimoles per litre (mmol/l) in the 35–64 age group. The results are age-standardized to minimize any effect of differing age structures on the apparent findings. See #38 Population Prevalence and Trends, #59 Age Standardization.**

3. **To convert to and from SI Units: 200 mg/dl = 5.17 mmol/l; 10 mmol/l = 387 mg/dl.**

4. **The graphs characterize men and women over a thirty-year age band in each survey for each population with a single value, but levels and trends vary with age. Age-specific data are published in the MONICA Data Book of population surveys, table 6.2.2 (1), and early results in MONICA Publication 11 (2).**

5. **Survey results could be influenced by failure to participate by some of those selected for the survey. The issue is complex. Different methods of recruitment and sampling were used in different populations. There is more than one definition of response rates. See #28 Sampling, #29 Recruitment and Response rates, MONICA Quality assessment of participation rates, sampling frames and fractions (1).**

6. **Cholesterol is one of the classic coronary risk factors, measured in blood as serum or plasma cholesterol. It is otherwise known as total cholesterol because it includes different fractions (such as low, intermediate and high-density lipoprotein, HDL-cholesterol). It is not influenced appreciably by time of day or fasting/non-fasting status, so it can be measured without special preparation.**

7. **Cholesterol was the only classical risk factor in MONICA dependent on the laboratory. Ensuring and maintaining comparability of different laboratories across ten years and 21 countries was a complex problem. Laboratory readings can drift. MONICA established a quality control centre for lipid measurement in Prague in the Czech Republic, which worked with its equivalent in Atlanta in the USA. See #33 Cholesterol, MONICA Manual Part III, Sections 1, 2 (1), MONICA Quality assessment of data on cholesterol (1), MONICA Quality assessment of data on awareness and treatment of cholesterol (1), the MONICA Data Book of population surveys, tables 6.2.1–6.2.7 (1), and MONICA Publication 13 (2).**

8. **Participants in the MONICA surveys consented to venepuncture. Blood was taken from an arm vein with minimal or no use of a tourniquet. It was analysed according to a written protocol as plasma or serum, for total and HDL-cholesterol, some being deep-frozen and stored for future reference. See #33 Cholesterol, MONICA Manual Part III, Sections 1, 2 (1).**

9. **The scale for men and women is the same. Mean cholesterol levels were similar in the two sexes. Compared with historical population differences there was relatively little variation between most populations, with mean readings ranging between 5.5 and 6.3 mmols/l. The population with the highest readings varied between men and women and the initial and final surveys. China-Beijing, CHN-BEI, see #55 had the lowest mean total cholesterol in all four graphs by a considerable margin.**

10. **The readings here are age-standardized so they conceal age differences. There is a steeper age gradient in women so that their cholesterol readings are lower than those in men of the same age at 35–44, but they are higher at age 55–64. Age-specific readings are given in the MONICA Data Book of population surveys, table 6.2.2 (1), and early results in MONICA Publication 11 (2).**

11. **The Data book contains tables covering a number of other data items concerning cholesterol, such as the percentage of participants above and below certain cut points, HDL-cholesterol, and in later surveys the reported frequency of earlier measurement and treatment. See the MONICA Data Book of population surveys, tables 6.2.1–6.2.7 (1). This Monograph discusses only total cholesterol. Despite our efforts, standardization for epidemiological comparison of measurement of HDL-cholesterol in the MONICA decade was unsatisfactory and failed to meet our criteria for formal publication. See MONICA Quality assessment of data on HDL-cholesterol (1).**

1. See Monograph CD-ROM or MONICA Website http://www.ktl.fi/monica/.
2. Full references and summaries of MONICA Publications appear in #85/86.
### Average Blood Cholesterol Concentration

#### Initial Risk-Factor Survey

<table>
<thead>
<tr>
<th>Country A</th>
<th>Country B</th>
<th>Mean Total Cholesterol in mmol/l</th>
</tr>
</thead>
<tbody>
<tr>
<td>FRA-LIL</td>
<td>SWI-VAF</td>
<td>4.5</td>
</tr>
<tr>
<td>FIN-KUO</td>
<td>FIN-NKA</td>
<td>5.0</td>
</tr>
<tr>
<td>CZE-CZE</td>
<td>SWE-NSW</td>
<td>5.5</td>
</tr>
<tr>
<td>ITA-FRI</td>
<td>GER-AU+</td>
<td>6.0</td>
</tr>
<tr>
<td>UNK-GLA</td>
<td>FIN-TUL</td>
<td>6.5</td>
</tr>
<tr>
<td>GER-AUR</td>
<td>SWE-GOT+</td>
<td>7.0</td>
</tr>
<tr>
<td>ICE-ICE</td>
<td>BEL-GHE+</td>
<td></td>
</tr>
<tr>
<td>BEL-CHA+</td>
<td>UNK-BEL+</td>
<td></td>
</tr>
<tr>
<td>LTU-KAU+</td>
<td>LTU-KAU+</td>
<td></td>
</tr>
<tr>
<td>GER-EGE+</td>
<td>DEN-GLO+</td>
<td></td>
</tr>
<tr>
<td>CAN-HAL+</td>
<td>FRA-TOU+</td>
<td></td>
</tr>
<tr>
<td>AUS-PER+</td>
<td>AUS-NEW+</td>
<td></td>
</tr>
<tr>
<td>SPA-CAT+</td>
<td>NEZ-AUC+</td>
<td></td>
</tr>
<tr>
<td>RUS-MOC+</td>
<td>SWI-TIG+</td>
<td></td>
</tr>
<tr>
<td>USA-STA+</td>
<td>RUS-NOS+</td>
<td></td>
</tr>
<tr>
<td>POL-TAR+</td>
<td>CHN-BEI+</td>
<td></td>
</tr>
</tbody>
</table>

#### Final Risk-Factor Survey

<table>
<thead>
<tr>
<th>Country A</th>
<th>Country B</th>
<th>Mean Total Cholesterol in mmol/l</th>
</tr>
</thead>
<tbody>
<tr>
<td>LTU-KAU+</td>
<td>SWI-TIG+</td>
<td>4.5</td>
</tr>
<tr>
<td>YUG-NOS+</td>
<td>YUG-NOS+</td>
<td>5.0</td>
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<td>CZE-CZE+</td>
<td>SWE-NSW+</td>
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<td>GER-BRE+</td>
<td>BEL-CHA+</td>
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<td>UNK-GLA+</td>
<td>FIN-TUL+</td>
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<td>GER-AUR+</td>
<td>SWE-GOT+</td>
<td>7.0</td>
</tr>
<tr>
<td>ICE-ICE+</td>
<td>BEL-GHE+</td>
<td></td>
</tr>
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<td>BEL-CHA+</td>
<td>UNK-BEL+</td>
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<td>LTU-KAU+</td>
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<tr>
<td>POL-TAR+</td>
<td>CHN-BEI+</td>
<td></td>
</tr>
</tbody>
</table>

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**RISK FACTORS: TOTAL BLOOD CHOLESTEROL**
Notes in italics are repeated to help random browsers—systematic readers should ignore them.

**G46**


2. The initial and final surveys did not take place exactly ten years apart. G46 incorporates corrections to standardize the differences, as if they were being measured across ten years.

3. Horizontal bars in G46 show the 95% confidence intervals around the estimated annual trend. The smaller the length of the bars, the more precise the trend estimate. If the bars fail to cross the zero line, the estimated trend is considered to deviate significantly from zero. Declining trends are shown to the left of the zero line, increasing trends, to the right.

4. To convert to and from SI Units: 200 mg/dl = 5.17 mmol/l; 10 mmol/l = 387 mg/dl.

5. Confidence intervals are similar for men and women; the population surveys sampled them in similar numbers.

6. G46 shows similar trends in total cholesterol in men and women, in the various populations. Two-thirds of the male populations show a decrease, tending to the left of zero. Ten show an increase, right of zero. In women, results are virtually the same, although specific populations vary a little in their ranking. Age-specific data are available in the MONICA Data Book on population surveys table 6.2.2 (1).

**G47**

7. G47 is a spot map showing the geographical distribution of the results shown in G46. Some of the confidence intervals in G46 include zero. These populations are marked with black spots. Those with a significant decrease in cholesterol levels are shown with blue spots while a significant increase is shown with a red spot. ‘Significant’ is statistical, meaning that the change is large enough for it to be unlikely to have arisen by chance when random sampling variation is taken into account. Significant changes and differences can occur through undetected bias, such as a drift in laboratory standards over time. These findings have not been adjusted for measurement quality.

8. Many populations show a significant decline in cholesterol between the initial and final surveys. Seven male and five female populations show an increase. There is some apparent geographical clustering of results.

9. Results shown here should be interpreted in association with the MONICA Quality assessment of data on total cholesterol (1), and with G56 (see later). The quality of total cholesterol data, despite intense attempts at standardization in the planning of MONICA, raises more questions than the quality of data on other risk factors. G56 shows that some of the more extreme cholesterol trends arose among population RUAs whose cholesterol quality scores were suboptimal. See notes on G56.

10. The only publication specific to cholesterol is MONICA Publication 13 (2) on data quality. MONICA Publication 11 (2) contained early cross-sectional and age-specific data. Further publications are in preparation and will be listed on the MONICA Website (1) as they appear.

1. See Monograph CD-ROM or MONICA Website http://www.ktl.fi/monica/.
2. Full references and summaries of MONICA Publications appear in #85/86.
G46 Ten-year change in average blood cholesterol concentration

Men

Women

G47 Spot maps of population changes in average blood cholesterol concentration

Significant increase
Insignificant change
Significant decrease
1. The timing of the initial and final surveys differed by population. They were usually eight to ten years apart but the interval could be as little as six years. The calendar years and months varied. See G10 and MONICA Quality assessment of age, date of examination and survey periods.

2. Results are shown as the mean body mass index (BMI) in kilograms per square metre for the 35–64 age group. See #34 Height, Weight, and Waist Circumference. The results are age-standardized to minimize any effect of differing age structures on the apparent findings. See #38 Population Prevalence and Trends, #39 Age Standardization.

3. The graphs characterize men and women over a thirty-year age band in each survey for each population with a single value, but levels and trends vary with age. Age-specific data are published in the MONICA Data Book of population surveys, table 6.3.4 (1), and early results in MONICA Publication 11 (2).

4. Survey results could be influenced by failure to participate by some of those selected for the survey. The issue is complex. Different methods of recruitment and sampling were used in different populations. There is more than one definition of response rates. See #28 Sampling, #29 Recruitment and Response Rates, MONICA Quality assessment of participation rates, sampling frames and fractions (1).

5. Body mass index is used as an indicator of obesity or body fat. Weight is corrected by the square of the body height. Although bone and muscle also contribute, the biggest variation between body mass in individuals, particularly in sedentary groups, is in their body fat. Epidemiologists have always been interested in the distribution of body fat, originally using calliper measurement of skin-fold thickness, but this was difficult to standardize. Measurement of abdominal obesity by waist circumference and its ratio with hip circumference became standard just too late for the MONICA protocol for the initial population surveys, although it was introduced into later MONICA surveys. Population surveys need simple techniques. Isotope tests, and weighing under water for body fat estimation can be done in laboratories but not in field surveys. See #34 Height, Weight, and Waist Circumference.

6. Participants had their weight and height measured with shoes and outside clothes removed. Measurement, as with blood pressure, appears simple and easy, but there is potential for problems in standardization of measurements, and of equipment, to ensure that population trends are genuine. See #34 Height, Weight, and Waist Circumference, MONICA Manual Part III, Section 1 (1), MONICA Quality assessment of data on weight and height (1), MONICA Quality assessment of data on waist and hip circumference (1).

7. The scale for men and women is the same. There was little variation between most population RUAs in the initial survey in men, except for China-Beijing, CHN-BEI, see #55, as previously for cholesterol. There was more variation in women. In the final survey there was again more variation between female populations than in men. Some populations show similar, and some rather different rankings between the two sexes, possibly related to differences in smoking levels by sex. Even a quick glance down the page shows that obesity is increasing between G48 and G49. This is confirmed when you turn the page to G50.

8. The MONICA Data Book of population surveys contains several tables 6.3.2–6.3.7 covering a number of items related to measurements of height, weight, body mass index, obesity cut points, waist and hip circumference and their ratio. Height itself is of epidemiological interest, as a marker of nutritional status in early life.

9. Obesity is not considered a major classical risk factor for coronary disease as are cigarette smoking, blood pressure and cholesterol, but it is of great importance for public health and has generated several papers in MONICA. See #34 Height, Weight, and Waist Circumference, MONICA Publications 27, 35, 37, 41 (2).

1. See Monograph CD-ROM or MONICA Website http://www.ktl.fi/monica/.
2. Full references and summaries of MONICA Publications appear in #85/86.
G48 Average body mass index (BMI) in the initial risk-factor survey

G49 Average body mass index (BMI) in the final risk-factor survey
Notes in italics are repeated to help random browsers—systematic readers should ignore them.


**G50**

2. The initial and final surveys did not take place exactly ten years apart, but this graph incorporates corrections to standardize the differences as if they were being measured across ten years.

3. Horizontal bars in G50 show the 95% confidence intervals around the estimated annual trend. The smaller the length of the bars, the more precise the trend estimate. If the bars fail to cross the zero line the estimated trend is considered to deviate significantly from zero. Declining trends are shown to the left of the zero line, increasing trends to the right.

4. Confidence intervals appear similar for men and women, although possibly a bit wider in more female populations. The population surveys sampled similar numbers of men and women.

5. G50 shows similar trends in body mass index in men and women in the various populations. The majority of male populations show an increase, so that the estimated trend is to the left of zero in only six populations, and to the right in the remainder. In women, there is a similar but less marked pattern with 15 populations showing a decline in body mass index, and the remainder an increase. Changes in women are more extreme at the top and bottom of the graphs than they are in men. Age-specific data are available in the MONICA Data Book of population surveys, table 6.3.4 (1).

**G51**

6. G51 is a spot map showing the geographical distribution of the results shown in G50. Some of the confidence intervals in G50 include zero. The populations concerned are marked by black spots. Those with a significant decrease in body mass index are shown with blue spots, while a significant increase is shown with a red spot.

7. Many populations show a significant increase in body mass index between the initial and final surveys. There is some apparent polarization of red and blue across Europe, particularly in women, but this is not consistent.

8. These results should be considered in association with the MONICA Quality assessment of data on weight and height, and with G56 (see later), which plots trends in population RUA results against their quality scores. These suggest that the population increases in body mass index shown here are real.

9. For further information see #34 Height, Weight, and Waist Circumference, MONICA Quality assessment of data on weight and height (1), MONICA Quality assessment of data on waist and hip circumference (1), MONICA Data Book of population surveys, tables 6.3.2–6.3.7 (1), MONICA Publications 27, 35, 37, 41 (2). Further publications are listed on the MONICA Website as they appear (1).

1. See Monograph CD-ROM or MONICA Website http://www.ktl.fi/monica/.
2. Full references and summaries of MONICA Publications appear in #85/86.
**G50 Ten-year change in average body mass index (BMI)**

*Men*

![Men BMI Ten-year trend graph]

**Women**

![Women BMI Ten-year trend graph]

**G51 Spot maps of population changes in average body mass index (BMI)**

*Men*

![Men BMI Spot maps]

*Women*

![Women BMI Spot maps]

Significant increase
Insignificant change
Significant decrease
1. The timing of the initial and final surveys differed by population. They were usually eight to ten years apart but the interval could be as little as six years. The calendar years and months varied. See G10 and MONICA Quality assessment of age, date of examination and survey periods (1).

2. Results are shown as the estimated average coronary risk-factor score in the 35–64 age group. The results are age-standardized to minimize any effect of differing age structures on the apparent findings. See #35 Risk-Factor Scores, #38 Population Prevalence and Trends, #39 Age Standardization.

3. The graphs characterize men and women over a thirty-year age band in each survey for each population with a single value, but levels and trends vary with age. Age-specific data are not published. The risk-factor score is derived from risk-factor data published in the MONICA Data Book of population surveys.

4. Survey results could be influenced by failure to participate by some of those selected for the survey. The issue is complex. Different methods of recruitment and sampling were used in different populations. There is more than one definition of response rates. See #28 Sampling, #29 Recruitment and Response Rates, MONICA Quality assessment of participation rates, sampling frames and fractions (1).

5. The risk-factor score is used to summarize the presumed contribution of the classical coronary risk factors: cigarette smoking, systolic blood pressure, and total cholesterol, along with body mass index, to coronary risk. The formula is based on follow-up or cohort studies in Europe in which thousands of subjects had such risk-factor measurements and were then followed-up for coronary events. Smoking, blood pressure and cholesterol contribute heavily to the score as classical major risk factors. The contribution of body mass index is smaller, particularly in women. See #35 Risk-Factor Scores, MONICA Publications 12, 32, 33, 38 (2), and Appendix to 38 published on the MONICA Website (1).

6. Although the scale for men and women is similar in G52 and G53, the scores differ on average by about 0.5 units between men and women. Populations rank similarly in men and women, but there are disparities. These may relate to sex differences in smoking rates, which are large in some population RUAs.

7. The risk-factor score is unique among the factors displayed in these charts, in that it is not the same for men and women. Although smoking levels differed in the two sexes, as did blood pressure sometimes, these did not account entirely for the lower score in women in G52 and G53. The statistical coefficients derived for men and women are different. Identical risk-factor values in the two sexes would produce lower scores in women. See #35 Risk-Factor Scores. Comparison of the sexes for this item is misleading.

8. The choice of a coronary risk-factor score for testing the MONICA risk-factor hypothesis involved considerable research and planning, some of which is published. See MONICA Publications 12, 32, 33, 38 (2) and the Appendix to publication 38 on the MONICA Website and Monograph CD-ROM. (1)

9. Coefficients for a stroke risk-factor score are similar but not identical. See #35 Risk-Factor Scores.

1. See Monograph CD-ROM or MONICA Website http://www.ktl.fi/monica/.
2. Full references and summaries of MONICA Publications appear in #85/86.
G52 Average coronary risk-factor score in the initial risk-factor survey

G53 Average coronary risk-factor score in the final risk-factor survey
Notes in italics are repeated to help random browsers—systematic readers should ignore them

G54
2. The initial and final surveys did not take place exactly ten years apart, but this graph incorporates corrections to standardize the differences, as if they were being measured across ten years.
3. Horizontal bars in G54 show the 95% confidence intervals around the estimated 10-year trend. The smaller the length of the bars the more precise the estimated trend. If the bars fail to cross the zero line the estimated trend is considered to deviate significantly from zero. Declining trends are shown to the left of the zero line, increasing trends to the right.
4. Confidence intervals are similar for men and women; the population surveys sampled them in similar numbers.
5. G54 shows similar trends in risk-factor scores between men and women in the various populations. The majority of male populations show a decrease, to the left of zero, in all but six populations. In women, there is a similar pattern with all but nine populations showing a decline in risk-factor score. Age-specific data are not published.

G55
6. G55 is a spot map showing the geographical distribution of the results shown in G54. Some of the confidence intervals in G54 include zero. The populations concerned are marked by black spots. Those with a significant decrease in risk-factor score are marked with blue spots, while a significant increase is shown with a red spot.
7. Most populations show a significant decrease in risk-factor score between the initial and final surveys. Only three in each sex show a significant increase.
8. The coronary risk-factor score is a derived variable. See MONICA Publications 12, 32 and 33 (2). The prime function of the risk-factor score was in testing the coronary risk factor, or First MONICA Hypothesis in MONICA Publication 38 (2). The quality scores of the risk factors contributing to the risk-factor score are summarized in the methodological appendix to MONICA Publication 38, published on the MONICA Website and MONICA CD-ROM (1).

1. See Monograph CD-ROM or MONICA Website http://www.ktl.fi/monica/.
2. Full references and summaries of MONICA Publications appear in #85/86.
G54 Ten-year change in average coronary risk-factor score

Men

Women

G55 Spot maps of population changes in average coronary risk-factor score

Men

Women

Significant increase
Insignificant change
Significant decrease
Risk factors: risk-factor quality scores

1. G56 shows scatter plots for the change in each risk factor against the quality score for that factor awarded after assessment of the data in the MONICA Quality assessment reports (1). See #12 Quality Assurance.

2. Quality scores covered items that could be assessed centrally from external quality control, from questionnaires completed by the investigators and from careful analysis of the data. A poor score was not a guarantee that results were unreliable. Conversely, a good score did not guarantee that results were not biased. There could be biases that had not been anticipated or could not be measured and assessed. In MONICA a score of 2.0 was awarded for data of acceptable and consistent quality with no major problems, 1.0 for data with minor problems or inconsistencies and 0.0 where there were significant problems that could not be solved retrospectively. A score of 0.0 is a bad score, but it does not of itself mean that data are unreliable, only that there is major concern about their quality.

3. Scoring was explicit and transparent, and done with the knowledge and cooperation of the investigators concerned. Quality problems are all discussed in the appropriate Quality assessment reports (1). Bias is more important than random error because it is average values that are being compared.

4. Ideally, the great majority of populations would achieve high scores, and the trends being measured would be large in relation to potential measurement errors. Populations with high scores would show the widest variation in risk-factor trends, so there would be no relation between poor scores and extreme results for trends.

5. The manuscript groups decided that MONICA could not exclude populations from hypothesis testing if a few data items were questionable, because almost all centres had some problem with one item or another. Instead it chose to incorporate quality scores into the collaborative analyses. See #12 Quality Assurance, MONICA Publication 38 (2), and its Appendix (1) published on the MONICA Website and CD-ROM.

6. Main results of hypothesis-testing appeared relatively insensitive to whether data quality scores were incorporated or not, and with what weighting. See MONICA Publications 38, 39 (2).

7. In G56 results appear satisfactory for smoking, blood pressure, and body mass index, and less than satisfactory for cholesterol.

8. Two populations with significant increase in total cholesterol between the initial and final surveys had the lowest quality score for this item.

9. Results of quality assessment for total cholesterol were not satisfactory. Those for HDL-cholesterol, not a core risk factor, but of great interest, were worse. This was despite involvement from the start of an external quality control centre, use of standard protocols and preliminary training, and testing with circulation of materials. Methods have advanced since the early 1980s, but standardization and quality control problems never disappear. Anyone denying their existence cannot have looked for them. Investigators in studies such as MONICA need to invest considerably in this area and should assume that they will have problems.

10. The WHO MONICA Project was ahead of its time in the 1980s in placing great emphasis on quality assurance. It also set a precedent by putting all its indicators of performance into the public domain by publishing them on its Website (1).

11. Quality scores aid the interpretation of individual trends. Along with estimates of precision, they were fundamental to the testing of the MONICA hypotheses by providing a means for involving different populations with differing reliability of data. See #40 Statistical Analysis—relating changes in risk factors and treatments to changes in event rates, MONICA Publication 38, 39 (2).

1. See Monograph CD-ROM or MONICA Website http://www.ktl.fi/monica/.
2. Full references and summaries of MONICA Publications appear in #85/86.
Scatter plots by population of change in risk factors against their quality scores

Daily cigarette smoking

Systolic blood pressure

Blood cholesterol concentration

Body mass index

RISK FACTORS: RISK-FACTOR QUALITY SCORES

Women

Men
Eight evidence-based treatments in coronary care

1. Basic coronary-event monitoring did not originally include any treatments or interventions. See G8. When MONICA was planned around 1980, it was not known whether acute coronary care was effective; most coronary deaths were sudden and untreated. The First MONICA, or coronary risk-factor Hypothesis seemed most relevant to disease trends. That acute care influenced survival in coronary events, (or its complement case fatality), was the basis of the Second MONICA or coronary care Hypothesis. The importance of cardiac drugs and treatment in secondary prevention was insufficiently appreciated.

2. For coronary care MONICA investigators were to record all relevant medication and interventions in coronary events for three phases of each coronary event: before the onset, after the onset during the pre-hospital and hospital period, and at discharge from hospital. A minimum of 500 consecutive cases was to be studied in two periods, near the start and at the end of coronary-event registration.

3. The 500 cases included large numbers both of untreated sudden deaths, in which there was difficulty in identifying previous medication, and also of non-fatal possible myocardial infarction, not included in MONICA case definition 1. See #23 Diagnosing Myocardial Infarction and Coronary Death. Coronary care data were most complete for non-fatal definite myocardial infarctions, a minority of the 500. Later it was agreed to monitor coronary care continuously, but data remained scanty from the first period.

4. The manuscript group examining the Second MONICA Hypothesis decided to study change in coronary care in non-fatal definite acute myocardial infarction across the two periods against change in major coronary end-points. Event rates, case fatality and mortality could not be measured in non-fatal cases alone, so a contemporaneous or overlapping period of full coronary-event registration was used.

5. The two periods of coronary care in each population, and associated but sometimes longer periods of coronary-event registration were shown in G11. Both coronary care, and coronary-registration periods are a sub-set of the data available. G11 showed that time periods are not the same, and distances between them are unequal, in different populations. Treatment changes are not standardized improvement rates, but simple differences. The manuscript group concentrated on eight evidence-based treatments.

6. G57 and G58 show change in use of beta-blockers, in cases of definite non-fatal myocardial infarction, between two time periods. A blue bar indicates increasing use, the left end is the treatment level per cent in the first period; the right end that in the second. Red bars indicate decreasing use, the right end is the treatment level per cent in the first period; the left end that in the second. The colourless gap to the left is common to both. Beta-blockers were widely used throughout the MONICA period. This explains why the blue and red bars begin a long way from zero.

7. G57 shows use of beta-blockers prior to myocardial infarction. Up to one half of new coronary events occur in those with previous angina pectoris, or myocardial infarction, in whom prior treatment might be expected. The other half would have no previous history of coronary heart disease, but some had hypertension. The scale maximum is 50%. G57 shows population RUAs with increasing but also decreasing use before infarction, possibly because of competing drugs for angina and hypertension.

8. G58 shows use during non-fatal definite myocardial infarction. The scale maximum is 100%. Use during infarction increased substantially in many but not all population RUAs as the findings of large randomized controlled trials fed through into practice. There is considerable heterogeneity.

9. Populations, listed alphabetically by country are those described in note 4c for G1 and G2. The asterisk for Swiss women marks missing data.

10. Beta-blockers are only one of numerous treatments and interventions that were recorded. See #24 Acute Coronary Care, MONICA Manual Part IV, Section 1, paragraph 4.1.4.3 (1), MONICA Quality assessment of acute coronary care data (1), the MONICA Data Book of coronary care, tables 11a-p, 12a-p, 13a-p (1), MONICA Publication 39 (2) the MONICA Second Hypothesis, or coronary care paper. The latter gives the denominators for each of these data points. Its Appendix, published on the MONICA Website (1) and Monograph CD-ROM, includes a review of why specific drugs were chosen for this analysis.

1. See Monograph CD-ROM or MONICA Website http://www.ktl.fi/monica/.
2. Full references and summaries of MONICA Publications appear in #85/86.
657 Change in beta blocker use before myocardial infarction

658 Change in beta blocker use during myocardial infarction
Notes in italics are repeated to help random browsers—systematic readers should ignore them.

1. See background notes at the beginning of this section, for G57 and G58, numbered 1–5.

2. G59 and G60 show change in use of antiplatelet drugs, (usually aspirin), in the treatment of definite non-fatal myocardial infarction, between two time periods. A blue bar indicates increasing use, the left end is the treatment level per cent in the first period; the right end that in the second. Red bars indicate decreasing use, the right end is the treatment level per cent in the first period, and the left end that in the second. The colourless gap to the left is common to both.

3. G59 shows change in use before myocardial infarction. Up to one half or so of coronary events occur in those with previous angina pectoris, or myocardial infarction, stroke or peripheral vascular disease in which prior treatment might be expected. The other half would have no such history so the scale maximum is 50%. Antiplatelet drugs were being introduced when MONICA began, both in acute care and in secondary prevention, but the impact on treatment of the major trials came while it was in progress. G59 shows that prior use was found to have increased to up to 30% of cases of non-fatal myocardial infarction coming into care. Specific changes in particular population RUAs should be cross-referenced with the time periods shown in G1 (1).

4. G60 shows use during non-fatal definite myocardial infarction. The scale maximum is 100%. Antiplatelet drugs were being introduced when MONICA began, both in acute care and in secondary prevention, but the impact of the major trials came while it was in progress. During MONICA monitoring of coronary care usage of these drugs increased by 70% in some populations making this the largest increase in use of any of the treatments we studied. Specific changes in particular population RUAs should be cross-referenced with the time periods shown in G1 (1).

5. Populations, listed alphabetically by country, are those in note 4c for G1 and G2. The asterisk for Swiss women marks absent data.

6. Antiplatelet drugs are only one of numerous treatments and interventions that were recorded. See #24 Acute Coronary Care, MONICA Manual Part IV, Section 1, paragraph 4.1.4.3 (1), MONICA Quality assessment of acute coronary care data (1), the MONICA Data Book of coronary care, tables 11a-p, 12a-p, 13a-p (1), MONICA Publication 39 (2) the MONICA Second Hypothesis, or coronary care paper. The latter gives the denominators for each of these data points. Its Appendix, published on the MONICA Website (1) and Monograph CD-ROM, includes a review of why specific drugs were chosen for this analysis.

1. See Monograph CD-ROM or MONICA Website http://www.ktl.fi/monica/.
2. Full references and summaries of MONICA Publications appear in #85/86.
G59 Change in antiplatelet (aspirin) use before myocardial infarction

G60 Change in antiplatelet (aspirin) use during myocardial infarction
Notes in italics are repeated to help random browsers—systematic readers should ignore them.

1. See background notes at the beginning of this section, for G57 and G58, numbered 1–5.

2. G61 and G62 show change in use of ACE inhibitor drugs (angiotensin-converting-enzyme inhibitors), in the treatment of definite non-fatal myocardial infarction, between two time periods. A blue bar indicates increasing use, the left end is the treatment level per cent in the first period; the right end that in the second. Red bars indicate decreasing use, the right end is the treatment level per cent in the first period, and the left end that in the second. The colourless gap to the left is common to both.

3. G61 shows change in use before myocardial infarction. Up to one half or so of coronary events occur in those with previous angina pectoris, or myocardial infarction, or other atheromatous disease, the other half would have no such history although some will have a history of hypertension. The scale maximum here is 50%. When MONICA began ACE inhibitor drugs were just about to be introduced, both in acute coronary care and in the treatment of hypertension and heart failure. The impact on treatment of the major trials came while it was in progress; recent suggestions of general use for secondary prevention of coronary heart disease postdated the MONICA study. G61 shows that prior use increased from almost zero to as much as 18% of cases of non-fatal myocardial infarction coming into care, presumably much of it for previously detected hypertension. Specific changes in particular population RUAs should be cross-referenced with the time periods shown in G11.

4. G62 shows use during non-fatal definite myocardial infarction. The scale maximum is 100%. ACE inhibitors were just about to be introduced when MONICA began, but the impact of the major trials on their use for left ventricular dysfunction during myocardial infarction came while it was in progress. During MONICA monitoring of coronary care, use of these drugs increased from low levels up to as much as 50% in some populations making this one of the larger increases in the use of the eight treatments we studied. The colourless gaps to the left of the blue bars in G62 suggest that ACE inhibitors were more widely used in men than women for myocardial infarction in the first period. Specific changes in particular population RUAs should be cross-referenced with the time periods shown in G11.

5. Populations, listed alphabetically by country, are those in note 4c for G1 and G2. The asterisk for Swiss women marks absent data.

6. ACE inhibitors are only one of numerous treatments and interventions that were recorded. See #24 Acute Coronary Care, MONICA Manual Part IV, Section 1, paragraph 4.1.4.3 (1), MONICA Quality assessment of acute coronary care data (1), the MONICA Data Book of coronary care, tables 11a-p, 12a-p, 13a-p (1), MONICA Publication 39 (2) the MONICA Second Hypothesis, or coronary care paper. The latter gives the denominators for each of these data points. Its Appendix, published on the MONICA Website (1) and Monograph CD-ROM, includes a review of why specific drugs were chosen for this analysis.

1. See Monograph CD-ROM or MONICA Website http://www.ktl.fi/monica/.
2. Full references and summaries of MONICA Publications appear in #85/86.
G61 Change in angiotensin converting enzyme (ACE) inhibitor use before myocardial infarction

G62 Change in angiotensin converting enzyme (ACE) inhibitor use during myocardial infarction
Notes in italics are repeated to help random browsers—systematic readers should ignore them.

1. See background notes at the beginning of this section, for G57 and G58, numbered 1–5.

2. G63 shows change in prior coronary artery revascularization and G64, change in use of thrombolytic therapy in the acute treatment of definite non-fatal myocardial infarction between two time periods. A blue bar indicates increasing use, the left end is the treatment level per cent in the first period; the right end that in the second. Red bars indicate decreasing use, the right end is the treatment level per cent in the first period; the left end that in the second. The colourless gap to the left is common to both.

3. G63 shows coronary artery revascularization procedures any time before the myocardial infarction being considered. Up to one half of coronary events occur in those with previous angina pectoris, or myocardial infarction, in which prior procedures might be expected. The other half would have no previous history of coronary heart disease. The scale maximum is 50%. Coronary artery bypass surgery was long established when MONICA began, but not common in most MONICA populations. It was supplemented by coronary angioplasty more recently. Prevalence of prior procedures in victims of heart attack is questionable as a measure of the use of such procedures in the general population, but it was the only measure available in the core data for MONICA. See #18 Health Services. G63 shows low prevalence in most populations and considerable disparities, but a net increase over time in the majority. Specific changes in particular population RUAs should be cross-referenced with the time periods shown in G11.

4. G64 shows use of thrombolytic drugs during non-fatal myocardial infarction. The scale maximum is 100%. Thrombolytic therapy was part of the coronary care revolution, occurring while MONICA was monitoring change. G64 shows a major increase in usage, not quite as much as for antiplatelet drugs, but from a lower level, in many populations. There is marked heterogeneity between populations, unlike antiplatelet drugs, perhaps reflecting the financial cost, and the complexity of administration, compared with aspirin. Specific changes in particular population RUAs should be cross-referenced with the time periods shown in G11.

5. Populations, listed alphabetically by country, are those in note 4c for G1 and G2. The asterisk for Swiss women marks absent data.

6. These are only two of numerous treatments and interventions that were recorded. See #24 Acute Coronary Care, MONICA Manual Part IV, Section 1, paragraph 4.1.4.3 (1), MONICA Quality assessment of acute coronary care data (1), the MONICA Data Book of coronary care, tables 11a-p, 12a-p, 13a-p (1), MONICA Publication 39 (2) the MONICA Second Hypothesis, or coronary care paper. The latter gives the denominators for each of these data points. Its Appendix, published on the MONICA Website (1) and Monograph CD-ROM, includes a review of why specific drugs were chosen for this analysis.

1. See Monograph CD-ROM or MONICA Website http://www.ktl.fi/monica/.
2. Full references and summaries of MONICA Publications appear in #85/86.
G63 Change in coronary artery revascularization (bypass graft or angioplasty) before myocardial infarction

G64 Change in thrombolytic drug use during myocardial infarction
1. In order to test the Second or coronary care Hypothesis, MONICA needed an index of coronary care equivalent to the risk-factor score used in the First Hypothesis.

2. The manuscript group was divided between those promoting a sophisticated score, incorporating carefully judged weightings of each component (Weighted Treatment Score), and those who wanted a simple pragmatic score reflecting implementation of evidence-based treatments (Equivalent Treatment Score). See #25 Treatment scores, and MONICA Publication 39 (2) Appendix. (1).

3. Both were tested. A strong correlation was found. The Weighted Treatment Score was strongly affected by one component, because of the heavy weighting given to it, prior coronary artery revascularization procedures (see G63). The simpler score was adopted.

4. The Equivalent Treatment Score, is simply one eighth of the sum of all eight of the treatments per cent, shown in G56 to G64. Three drug groups, beta-blockers, antiplatelet, and ACE-inhibitors, score twice each, once for use before the onset of myocardial infarction, and once for use afterwards. Treatments at hospital discharge were not included in the score but would have been very highly correlated with use in the event.

5. The Equivalent Treatment Score has the greatest contribution from treatments that changed most, in absolute percentage terms, between the two coronary care periods in MONICA. The leader was antiplatelet drugs (aspirin), during the attack (see G60).

6. G65 shows populations listed alphabetically by country, as in previous treatment graphs. The asterisk for Swiss women indicates missing data. G66 shows their ranking by change between the two coronary care periods, as in earlier formats.

7. Note that maximum change in G65, giving a high rank in G66 implies a low start and a high finish point. Populations could rank highly for either or both of these reasons. The actual finishing score was similar in many populations, some of which started with a high score, and therefore ranked only for moderate change. G65 needs to be studied with G11, and with MONICA Publication 39 (2), which tabulates numbers and time periods precisely. Differences in population RUAs with high finishing scores from other treatments were often influenced by discrepancies in their use of beta-blockers during infarction in the second period (see G58).

8. Inequality of coronary care periods and the distance between them inhibit simple comparison of the rate of introduction of new therapies. It did not affect the testing of the coronary care hypothesis because endpoint changes were compared for similar periods. See later section, G77.

9. The rate of introduction of different therapies can be compared using the MONICA Data Book of coronary care tables 11, 12, 13 (1). Treatments tended to be introduced fairly rapidly in a non-linear manner. Only a minority of populations, however, have treatment data for all their years of registration. Years are grouped in the Data Book.

10. Graphs here and the tables in MONICA Data Book on coronary care, tables 11a-p, 12a-p, 13a-p and in MONICA Publication 39 (2), show no significant sex bias in the use of evidence-based medication in definite myocardial infarction in the MONICA population RUAs over the decade that was studied. This is despite widespread reporting in the literature of the existence of such a problem. This question is being analysed in a paper being prepared at the same time as this Monograph.

11. Further papers on coronary care are in preparation at the time of writing the Monograph. They will be listed on the MONICA Website as they appear (1).

1. See Monograph CD-ROM or MONICA Website http://www.ktl.fi/monica/.
2. Full references and summaries of MONICA Publications appear in #85/86.
665 Change in Equivalent Treatment Score

Men

Women

666 Populations ranked by change in Equivalent Treatment Score

Men

Women
1. These scatter plots are part of the procedures for testing MONICA findings to see if they are likely to be genuine, or unduly influenced by variations in data quality.

2. A data quality score for coronary care was derived from a number of items. See #12 Quality Assurance, MONICA Quality assessment of acute coronary care data, (1) MONICA Publication 39 (2), Appendix (1), (published on MONICA Website and on the Monograph CD-ROM). Such items included the frequency with which coronary care records were missing when they should have been completed, and the frequency with which data were coded as not known, along with other items. The acute coronary care quality score is the same for both sexes in each population RUA.

3. Changes in treatments during the MONICA study period were very large in relation to possible sources of error.

4. Both the greatest and the least changes in Equivalent Treatment Score occurred in populations with high scores for data quality. There were few poor scores for data quality. These were associated with the middle range of treatment changes.

5. It is therefore unlikely that MONICA findings on coronary care are significantly affected by data quality.

6. This shows the geographical distribution of changes in the Equivalent Treatment Score. Large treatment changes are shown in blue while modest ones are shown in red. There is a more striking geographical polarization of results than for any of the previous MONICA spot maps.

7. The previous warning, that unequal periods and different times are being compared, is still true. Examination of G11 however, shows that while a late first coronary care recording period and early second period does apply to some red spot populations (in Germany-East Germany, GER-EGE, #65, they were close together) it does not apply to most. The geographical polarization is therefore real.

8. The polarization of results does raise problems for interpretation of the coronary care hypothesis (see later). If populations are clustered together, can they be considered independent in terms of statistical testing? What else might be happening? See discussion in MONICA Publication 39 (2).

1. See Monograph CD-ROM or MONICA Website http://www.ktl.fi/monica/.
2. Full references and summaries of MONICA Publications appear in #85/86.
**G67 Scatter plot of change in Equivalent Treatment Score against the acute coronary care quality score**

Men

![Scatter plot for men](image)

Women

![Scatter plot for women](image)

**G68 Spot maps of population changes in Equivalent Treatment Score**

Men

![Spot map for men](image)

Women

![Spot map for women](image)

- < 15% change
- >= 15% change
Hypotheses: coronary disease and coronary risk factors

1. The following four graphs were plotted during the testing of the First MONICA, or coronary risk-factor Hypothesis, about the association between change in coronary risk factors and change in coronary-event rates. The detailed presentation, along with these graphs, is found in MONICA Publication 38 (2). Much of the technical discussion is in its Appendix, published on the MONICA Website and the Monograph CD-ROM (1). See also #2 MONICA Hypotheses and Study Design, #35 Risk-Factor Scores, #40 Statistical Analysis—relating changes in risk factors and treatments to changes in event rates.

2. Each coloured point in the plots identifies the location of a MONICA population RUA. It shows how much its risk factors changed in ten years on the x-axis, and how much its event rates changed on the y-axis. Populations are identified in G69 and G70 by their abbreviated 2-letter codes in place of the seven-character identifications, one letter for country, and one for population. See Appendix and #51–83.

3. A strong simultaneous association between any change in the coronary-risk score, calculated from changing levels of classical risk factors, and changes in coronary-event rates in the same populations would result in the MONICA populations being arranged along a gradient, or regression line from near the bottom left corner of each plot towards the top right. Calculated regression lines, their equations and 95% confidence limits are added to G69 and G70.

G69

4. The results in G69 come from the whole registration period. They show a modest relation between changes in the risk-factor score and changes in coronary events but also a considerable scatter of populations. At any level of change in the risk-factor score there is considerable variation in the trends in coronary-event rates. Results in men might be considered more precise than in women because of their larger number of coronary events but the gradient of the calculated regression line is small. The variation in the trends in coronary-event rates is badly predicted from the trends in risk factors. In addition a two per cent per year reduction in coronary-event rates is predicted when there is no change in the risk-factor score. The gradient of the regression line in women is more positive, but the MONICA populations are still very scattered about the graph.

5. G70 shows what happens when a lagged (= delayed) registration period is used (see G8). The justification is that change in risk factors must precede a decline in coronary risk, perhaps by a number of years. A time lag was introduced for the beginning of the study period, but not for the end, because most of the final surveys were done at that time or after the end of the event registration periods. Results still show considerable scatter of populations, but the gradients of the regression lines are now considerably steeper. See MONICA Publication 38 (2), for a full discussion of the rationale for the lagged registration period.

6. These graphs provoked considerable discussion. Results neither prove nor disprove the coronary risk-factor hypothesis. They can be used to assess the potential contribution of risk-factor change to changing coronary-event rates in whole populations, but there is considerable uncertainty. This leaves potential room for other risk factors or determinants of trends in coronary-event rates, but without actually proving that they exist. One of these is probably drug treatment, see G77.

7. For further information see MONICA Publication 38 (2), its appendix on the MONICA Website (1) and CD-ROM, the subsequent Lancet correspondence and citations of this paper.

1. See Monograph CD-ROM or MONICA Website http://www.ktl.fi/monica/.
2. Full references and summaries of MONICA Publications appear in #85/86.
First MONICA Hypothesis: change in coronary-event rates against change in coronary risk-factor score, full registration period

Men

\[ y = -2.19 + 0.17x \]

Women

\[ y = -0.69 + 0.34x \]

First MONICA Hypothesis: change in coronary-event rates against change in coronary risk-factor score, lagged registration period

Men

\[ y = -2.33 + 0.46x \]

Women

\[ y = -0.37 + 0.56x \]
1. These graphs should be looked at in association with the notes on G69 and G70.

2. Coronary risk is known to be multi-factorial, so that the effect of one risk factor will be confounded and modified by what is happening to the others. G71 and G72 show changes in coronary-event rates in different populations, in relation to the change in single risk factors, without any correction for the effects of the others. See #35 Risk-Factor Scores. Populations are not individually identified, as they were in G69 and G70. Coloured spots are used to mark them. Because the same population results are used in each graph, their positions along the y-axis will be constant for each sex and registration period, but the position on the x-axis will vary with the risk factor concerned. Calculated regression lines have been added but without the accompanying equation or 95% confidence limits.

G71

3. G71 uses the full registration period. Again there is considerable variation in the change in coronary-event rates of populations for any given change in risk factor, without any clear overall pattern. Gradients are rather flat or even negative in the case of body mass index, but five of the eight graphs show a positive gradient for the regression line. In each risk-factor plot the majority of populations show a trend in one direction (usually decreasing). The regression line may be strongly influenced by one or two outlying populations at the other extreme (increasing, but with body mass index, reversed).

G72

4. G72 uses the lagged (= delayed) registration period explained in the notes on G70 and shown in G8. The pattern of the scatter plots and the associated regression lines do change but not in a consistent manner. These graphs should be studied in association with MONICA Publication 38 (2) where the contribution of each individual risk factor is estimated in the tables. There is detailed discussion of how the manuscript group interpreted the results in the paper. There were contributions from others in the subsequent correspondence and citations that followed it. Technical information is found in the appendix on the MONICA Website and CD-ROM (1). See MONICA Web Publication 20.

1. See Monograph CD-ROM or MONICA Website http://www.ktl.fi/monica/.
2. Full references and summaries of MONICA Publications appear in #85/86.
G71 First MONICA Hypothesis: change in coronary-event rates against change in individual coronary risk factors, full coronary-event registration period

HYPOTHESES: CORONARY DISEASE AND CORONARY RISK FACTORS

G72 First MONICA Hypothesis: change in coronary-event rates against change in individual coronary risk factors, lagged coronary-event registration period
Hypotheses: stroke and stroke risk factors

Notes in italics are repeated to help random browsers—systematic readers should ignore them

1. The next four graphs were plotted during the testing of the First MONICA stroke, or risk-factor Hypothesis, concerning the association between changes in cardiovascular risk factors and change in stroke-event rates. A manuscript containing these graphs was in preparation for publication at the same time as this Monograph, linked with a technical appendix similar to MONICA Publication 38 (2) for coronary events and its Appendix (1), MONICA Web Publication 20. This analysis is very much in parallel with that for coronary disease. See MONICA Publication 45 and MONICA Web Publication 30, and also #2 MONICA Hypotheses and Study Design, #35 Risk-Factor Scores, #40 Statistical Analysis—relating changes in risk factors and treatments to changes in event rates.

2. Each coloured point in the plots identifies the location of a MONICA population RUA, showing how much its risk factors changed in ten years on the x-axis, and how much its event rates changed on the y-axis. Populations are identified in G73 and G74 by their abbreviated 2-letter codes in place of the seven-character identifications, one letter for country, and one for population. See #90 Appendix and #51–83. The number of stroke population RUAs is only 40% of the number for coronary-event registration. The precision with which trends in stroke-event rates can be estimated within each population is limited by the numbers of strokes in the 35–64 age group.

3. A strong simultaneous relation between any change in the stroke-risk score, calculated from changing levels of classical risk factors, and related changes in stroke-event rates in the same populations would result in the MONICA populations being arranged along a gradient, or regression line from near the bottom left corner of each plot towards the top right. Calculated regression lines, their equations and 95% confidence limits are added to G73 and G74. Note that the scale of the y-axis in the stroke graphs is different from that in the preceding graphs G69–G72 for coronary disease. This distorts simple visual comparison of the gradients of regression lines, but not whether they are positive or negative.

G73

4. The analysis in G73 used the whole registration period. It fails to show any meaningful relation between changes in the risk-factor score and changes in stroke event rates in men as the gradient is virtually flat. At any level of change in the risk-factor score there is considerable variation in the trends in stroke-event rates. Results in women are different in that the calculated regression line shows a positive gradient. Both plots show little change in predicted stroke-event rates when there is no change in the risk-factor score. The number of data points is limited and it is possible to argue that results in both men and women may be being influenced by a small number of outlying populations. However, sensitivity analyses have not shown that re-analysis using different weightings for data quality scores, or omitting certain populations make a significant effect on the results of these findings, so they are comparatively robust.

G74

5. G74 shows what happens when a lagged (= delayed) registration period is used (see G9). The justification is that change in risk factors must precede a decline in stroke risk, perhaps by a number of years. A time lag was introduced for the beginning of the study period, but not for the end, because most of the final surveys were done at that time or after the end of the event registration periods. Results still show considerable scatter of populations. The gradients of the regression lines are now considerably steeper than in G73. That for women shows a more strongly positive or increasing trend with increase in risk-factor score. That for men shows a more strongly negative or decreasing trend with increasing risk-factor score. These results are contradictory and difficult to explain. Comparison shows that certain population RUAs had contrasting stroke-rate trends in men and women although their risk-factor changes were similar.

6. Interpretation of these graphs is a matter for discussion. The MONICA study was designed primarily to investigate and explore trends in coronary-event rates in male populations. For stroke results it was under-powered both in numbers of populations and in its ability to measure trends in event-rates with precision. It appears from these results that stroke risk-factor scores, used for estimating stroke risk in individuals, are less successful in predicting or explaining changes in the risk of stroke in whole populations. See MONICA Publication 45.

1. See Monograph CD-ROM or MONICA Website http://www.ktl.fi/monica/.
2. Full references and summaries of MONICA Publications appear in #85/86.
G73 First MONICA stroke Hypothesis: change in stroke-event rates against change in stroke risk-factor score, full stroke-event registration period

Men

Women

G74 First MONICA stroke Hypothesis: change in stroke-event rates against change in stroke risk-factor score, lagged stroke-event registration period

Men

Women
Notes in italics are repeated to help random browsers—systematic readers should ignore them

1. These graphs should be looked at in association with the notes on G73 and G74.

2. Although related strongly to blood pressure, stroke risk is multi-factorial, so the effect of one risk factor will be confounded and modified by what is happening to the others. The weighting of cardiovascular risk factors for a stroke risk score is different from that for coronary events. See #35 Risk-Factor Scores. G75 and G76 show changes in stroke-event rates in different populations, in relation to the change in single risk factors, without any correction for the effects of the others. Populations are not individually identified as they were in G73 and G74. Coloured spots are used to mark them. Because the same population results are used in each graph, their position along the y-axis will be constant for each sex and registration period, but the position on the x-axis will vary with the risk factor concerned.

3. G75 uses the full stroke-event registration period. There is considerable variation in the estimated trends in stroke rates, as seen in the previous graphs. Change in individual risk factors does not seem to be an effective method of explaining this variation. The calculated regression line is virtually flat for three of the risk factors in men, and negative for the fourth, body mass index. In women there is a positive gradient for three factors, although weak in relation to the trends that were observed, but a weak negative gradient for cigarette smoking.

4. G76 uses the lagged (= delayed) period, explained in notes on G74 and shown in G9. There is no obvious change in the results in men other than that the negative slope of the calculated regression line in body mass index becomes more negative. In women, as in G73 and G74 the results are again rather contradictory. This is not surprising given the contradictory trends in some population RUAs for men and women for similar risk-factor results. Change in cigarette smoking shows no effect on stroke rates but change in blood pressure, total cholesterol and body mass index all show gradients in the expected positive direction. Of these the most important contribution, and the most predictable from the literature, is for change in systolic blood pressure. It is difficult to explain why there is no similar effect in men.

5. These results are a matter for debate. They are discussed in MONICA Publication 45. One contributory factor may be the geographical origin of the populations concerned. Changes in stroke rates occurred in eastern Europe at a time of severe economic upheaval unaccompanied by major changes in cardiovascular risk factors. These populations accounted for nearly half of those in this study.

6. For further information on the general problem of these analyses with respect to coronary and stroke events see MONICA Publications 38 and 45 (2) and the Appendices (1), MONICA Web Publications 20 and 30.
HYPOTHESES: STROKE AND STROKE RISK FACTORS

**G75** Change in stroke-event rates against change in individual stroke risk factors, full stroke-event registration period

![Graphs showing the relationship between various risk factors and stroke-event rates for men and women.](image)

**G76** Change in stroke-event rates against change in individual stroke risk factors, lagged stroke-event registration period

![Graphs showing the relationship between various risk factors and stroke-event rates for men and women.](image)

**Table showing the average annual trend in BMI, smoking, and cholesterol for men and women.**

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average annual trend in BMI (kg/m²)</td>
<td>-0.3, -0.2, -0.1, 0, 0.10</td>
<td>-0.3, -0.2, -0.1, 0, 0.1</td>
</tr>
<tr>
<td>Average annual trend in smoking (%)</td>
<td>-1.5, -1, -0.5, 0, 0.5, 1, 1.5, 2</td>
<td>-6, -4, -2, 0, 2</td>
</tr>
<tr>
<td>Average annual trend in smoking (%)</td>
<td>-1.5, -1, -0.5, 0, 0.5, 1, 1.5, 2</td>
<td>-6, -4, -2, 0, 2</td>
</tr>
<tr>
<td>Average annual trend in cholesterol (mmol/l)</td>
<td>-0.1, -0.05, 0, 0.05, 0.1</td>
<td>-0.1, -0.05, 0, 0.05, 0.1</td>
</tr>
<tr>
<td>Average annual trend in cholesterol (mmol/l)</td>
<td>-10, -8, -6, -4, -2, 0, 2</td>
<td>-10, -8, -6, -4, -2, 0, 2</td>
</tr>
<tr>
<td>Average annual trend in systolic blood pressure (mm Hg)</td>
<td>-1.5, -1, -0.5, 0, 0.5, 1, 1.5, 2</td>
<td>-2, -1.5, -1, -0.5, 0, 0.5, 1, 1.5, 2</td>
</tr>
<tr>
<td>Average annual trend in systolic blood pressure (mm Hg)</td>
<td>-10, -8, -6, -4, -2, 0, 2</td>
<td>-10, -8, -6, -4, -2, 0, 2</td>
</tr>
<tr>
<td>Average annual trend in total cholesterol (mmol/l)</td>
<td>-0.1, -0.05, 0, 0.05, 0.1</td>
<td>-0.1, -0.05, 0, 0.05, 0.1</td>
</tr>
<tr>
<td>Average annual trend in total cholesterol (mmol/l)</td>
<td>-10, -8, -6, -4, -2, 0, 2</td>
<td>-10, -8, -6, -4, -2, 0, 2</td>
</tr>
</tbody>
</table>
Hypotheses: coronary care

1. G77 shows the results of the analyses made to test the Second MONICA, or coronary care Hypothesis, relating changes in treatment of coronary events to changes in case fatality, and subsequently to changes in coronary-event rates and mortality rates. They were published and discussed in MONICA Publication 39 (2), and its methodological Appendix (1). See also the subsequent Lancet correspondence.

2. Trends in end-points were in G15, G18 and G22; in treatments and Equivalent Treatment Score in G57–G66. Populations are as for the latter (abbreviations on the following page); time periods as in G11.

3. The MONICA coronary care hypothesis relates increasing treatment with decreasing coronary end-points. If there is an effect, the fitted regression lines and equations (along with the 95% confidence limits) should show decreasing or negative gradients.

4. The original hypothesis was framed in terms of acute coronary care and 28-day case fatality. This is tested in G77a. Most coronary deaths occur out of hospital and are not treated in the attack. Analyses are possible to see whether it is the hospital or pre-hospital component of deaths that are declining—the latter would emphasize secondary prevention rather than acute care.

5. The eight evidence-based treatments we examined were highly correlated so we could not apportion responsibility for the observed benefits. It is even conceivable in this observational study of whole populations (an 'ecological analysis') that extraneous unmeasured factors might have been responsible. See discussion in MONICA Publication 39, and the subsequent correspondence and citations.

6. The manuscript group examined other coronary end-points. There was a significant association between treatment change and change in coronary-event rates, and a stronger one still for change in mortality rates. See G77b and G77c. The results are very strongly positive.

7. There is a relation between change in mortality and associated change in case fatality and coronary-event rates. (See discussion of G22 and G23). The original hypotheses related risk factors to coronary-event rates, and treatments to case fatality. The results of the initial analyses of trends in end-points, see G23, suggested that case fatality had less effect on mortality trends than did event rates. It was a puzzle therefore that new treatments are more strongly related to change in mortality rates than they are to case fatality—and that an effect of change in risk factors has been more difficult to demonstrate.

8. In retrospect it is not surprising that the systematic introduction of powerful drugs on a large scale by sophisticated health-care systems had a more measurable impact on coronary end-points than that of the population changes in risk factors, which were small and difficult to measure. In another decade results could be different. Risk factors are now under pharmacological attack.

9. Some MONICA populations had good information but most were unable to provide data for sudden coronary deaths on previous history and medication. MONICA as a whole could not separate first presentations of coronary disease, susceptible to risk-factor change, from disease progression where drugs for secondary prevention are important. Analyses in individual populations, although worth doing, will lack the power of the MONICA collaboration.

10. MONICA results on change in coronary end-points are polarized between east and west (see G24, G25), as are those for treatment (see G67, G68), complicating interpretation of their association.

11. Analyses for the MONICA First and Second Coronary Hypotheses, MONICA Publications 38 and 39 (2), are still to be integrated. It will be necessary to define population RUAs that can be analysed for both studies together, and plan how to cope with a time-lag for risk factors, but not for coronary care. New MONICA publications on this and other subjects will be listed on the MONICA Website as they appear.

1. See Monograph CD-ROM or MONICA Website http://www.ktl.fi/monica/.
2. Full references and summaries of MONICA Publications appear in #85/86.
**G77a Second MONICA Hypothesis: change in case fatality against change in Equivalent Treatment Score**

Men

![Graph showing the relationship between change in case fatality and change in Equivalent Treatment Score for Men. The equation is $y = 12.1 - 0.96x$.]

Women

![Graph showing the relationship between change in case fatality and change in Equivalent Treatment Score for Women. The equation is $y = 7.8 - 0.8x$.]

**G77b Second MONICA Hypothesis: change in coronary-event rates against change in Equivalent Treatment Score**

Men

![Graph showing the relationship between change in coronary-event rate and change in Equivalent Treatment Score for Men. The equation is $y = 7.6 - 1.27x$.]

Women

![Graph showing the relationship between change in coronary-event rate and change in Equivalent Treatment Score for Women. The equation is $y = 9.0 - 1.14x$.]

**G77c Second MONICA Hypothesis: change in MONICA coronary heart disease (CHD) mortality rates against change in Equivalent Treatment Score**

Men

![Graph showing the relationship between change in CHD mortality rate and change in Equivalent Treatment Score for Men. The equation is $y = 18.7 - 2.11x$.]

Women

![Graph showing the relationship between change in CHD mortality rate and change in Equivalent Treatment Score for Women. The equation is $y = 13.5 - 1.69x$.]