Prevalence of ischemic resting and stress electrocardiographic abnormalities and angina among 40- to 59-year-old men in selected U.S. and U.S.S.R. populations


ABSTRACT The prevalence of electrocardiographic (ECG) abnormalities and angina was investigated in 40- to 59-year-old men from two samples, one from a U.S.S.R. study in two locations and one from a U.S. study in nine locations. ECG abnormalities were defined by the Minnesota code and angina was defined by the Rose questionnaire. No differences were found in the prevalence of major Q waves and major or minor ischemia between the two samples, but differences were found in specific indicators of major ischemia. Major ischemic changes were more prevalent in older subjects in both samples. Estimated prevalence of angina was 50% less in the U.S. sample than in the U.S.S.R. sample, and this was consistent with the proportion of subjects excluded from the exercise test because of angina. In both samples, subjects with ECG abnormalities had higher systolic blood pressures. No difference in exercise test abnormalities was found between samples; however, more subjects with a history compatible with coronary artery disease were excluded from the U.S.S.R. sample. Circulation 77, No. 2, 270-278, 1988.

THE PROBLEM of coronary artery disease (CAD) is an important one, particularly in economically developed countries, where epidemiologic studies have demonstrated a high prevalence of coronary events, accounting for more than one-third of all male deaths in many industrialized nations. The chronic nature of atherosclerotic cardiovascular disease and the late development of symptoms make effective prevention difficult. Epidemiologic studies have demonstrated that certain factors, such as the level of blood pressure or cholesterol, increase the risk of developing CAD. These risk factors, however, may have different associations with disease development in different geographic areas, as found in northern and southern Europe. A comparison of the presence and magnitude of cardiovascular risk factors between countries and their association with evidence for CAD should depict the relative importance of these factors.

Cross-sectional surveys in western Europe, eastern Europe, the United States, and Israel using the Minnesota Code indicate that approximately 5% of middle-aged men exhibit electrocardiographic (ECG) changes suggestive of ischemia, but marked differences in the prevalence of ECG abnormalities between populations have been found. Differences in the prevalence of CAD have also been detected by means of the Rose questionnaire to diagnose angina.

In 1972 the governments of the United States and the Union of Soviet Socialist Republics signed an agreement that led to the implementation of the U.S. and U.S.S.R. Joint Program in Cardiovascular Disease. Studies in Cardiovascular Area 1 began in 1973 and represent the careful construction of a large collaborative program as part of the Prevalence Study of the Lipid Research Clinics (LRC) Program. This article focuses on the prevalence of ECG abnormalities and angina as diagnosed by the Rose questionnaire in 40- to 59-year-old men from selected samples from U.S. and U.S.S.R. populations and presents a univariate analysis...
analysis of the risk factors for coronary heart disease in relation to ECG findings.

Methods

The data used in this analysis were collected as part of the Joint US-USSR LRC Program Prevalence Study.13, 18-20 Participants were selected from nine well-defined target subpopulations in the U.S. and two in the U.S.S.R. (Table 1). These subpopulations cover a broad range of geographic, cultural, socioeconomic, demographic, and ethnic groups, but they are not necessarily representative of either country. Therefore, the results, although adding to the understanding of heart disease, may not be the same as those found in a probability sample selected from the entire population of either the U.S. or the U.S.S.R.

Screening visits. The Prevalence Study involved two sequential examinations. Visit 1 was a brief screening to obtain information on age, sex, ethnicity, occupation, education, history of usage of five lipid-altering medications, and blood samples for determination of fasting plasma total cholesterol and triglyceride levels. In addition to this basic set of information, clinics in the U.S.S.R. collected height, weight, blood pressure, triceps skinfold, resting ECGs, and high-density lipoprotein (HDL) cholesterol measurements, and administered the Rose questionnaire for angina.

A 15% random sample of visit 1 participants was asked to return for the more extensive visit 2 examination. In addition, all persons who had elevated lipid levels or who were taking lipid-lowering medication (10% to 15% of visit 1 participants) were asked to return. Thus, visit 2 participants were almost equally divided between those randomly selected and those with elevated lipid levels or taking lipid-lowering medication.21, 22 The visit 2 examination typically took place 2 to 6 weeks after the visit 1 screening and included six major components: the basic visit 2 interview (personal and family histories relevant to vascular disease and detailed medication use history), lipid and lipoprotein cholesterol determinations, blood pressure and anthropometric measurements, resting and exercise ECGs, the 24 hr dietary recall, and nonlipid clinical chemistries.

Standardization of procedures. Standardization of all collaborative activities within the LRC Program was made possible by a common protocol with detailed documentation of procedures, by training and certifying all data collection personnel, and by regular monitoring of data collection and quality. Interviews were conducted in English in the U.S. and in Russian in the U.S.S.R., which meant that forms had to be translated and minor changes in content resulted. Whenever possible, WHO translations such as for the Rose questionnaire for angina were used. Edit and error correction procedures were instituted at a central facility in each country; furthermore, all data from both countries were reviewed, processed, and analyzed at a common data coordinating center at the University of North Carolina.

Laboratory measurements. A detailed description of the laboratory procedures is provided in the LRC Manual of Laboratory Operations.23 The LRC protocol required that blood specimens be obtained from participants who had fasted for at least 12 hr. Venipuncture was done with the examinees in a sitting position; a tourniquet was used but was released before collection of the blood sample to prevent an artifactual increase in the concentration of plasma lipids. All samples were cooled immediately on wet ice, and standardized lipid laboratory procedures were initiated within 3 hr after venipuncture. Ultra-centrifugation at saline density d = 1.006 g/ml was performed to yield a supernatant fraction containing very low-density lipoprotein (VLDL) cholesterol and an infranatant fraction containing both low-density lipoprotein (LDL) cholesterol and HDL cholesterol. HDL cholesterol was measured directly from total plasma after precipitation of the apo-B-containing lipoproteins by means of heparin and manganese chloride. An estimation of VLDL was obtained by dividing the total plasma triglyceride by five. LDL was then calculated by subtracting the directly measured HDL cholesterol value and the estimated VLDL value from the total cholesterol level. Plasma total cholesterol and triglyceride levels were estimated by a two-step method, includ-

<p>| TABLE 1 |
| Sampling frames and population descriptions |</p>
<table>
<thead>
<tr>
<th>Sampling frame</th>
<th>Clinic Name</th>
<th>Target population description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Occupational groups</td>
<td>Seattle</td>
<td>Employees of Pacific Northwest Bell Telephone Co., ages 20-65, working in King County, WA, as of July 15, 1972</td>
</tr>
<tr>
<td></td>
<td>Stanford</td>
<td>Stanford University employees, ages 26-70, working at least half-time as of March 1, 1972</td>
</tr>
<tr>
<td>Households</td>
<td>Iowa</td>
<td>Adults ages 25-59 residing in Cedar County, IA, as of July 1, 1973</td>
</tr>
<tr>
<td></td>
<td>Johns Hopkins</td>
<td>Columbia, MD – adults, children, and relatives living in the same household, who were members of the Columbia Medical Plan between 1973-1975</td>
</tr>
<tr>
<td></td>
<td>La Jolla</td>
<td>Residents as of August 2, 1972, of Rancho Bernardo, CA, ages 12 or older</td>
</tr>
<tr>
<td></td>
<td>Minnesota</td>
<td>Residents ages 10-59 of four census tracts in Richfield between May 1, 1973, and April 30, 1974</td>
</tr>
<tr>
<td></td>
<td>Oklahoma</td>
<td>Residents 18 and older living in Canadian, McClain, Lincoln, or Potawatomie counties as of April 1, 1972</td>
</tr>
<tr>
<td>Schoolchildren &amp; their parents</td>
<td>Baylor</td>
<td>Sophomore high school students in the Houston Independent School District between 1972-1975, and their parents</td>
</tr>
<tr>
<td></td>
<td>Cincinnati</td>
<td>Students and their parents enrolled in the Princeton School District during 1973-1974 in grades 1, 3, 5, 7, 9, 11, &amp; 12</td>
</tr>
<tr>
<td></td>
<td>Voting lists</td>
<td>Men born in 1916-1935 residing in the Oktyabrskii District by the 1974 voting lists</td>
</tr>
<tr>
<td></td>
<td>Moscow</td>
<td>Men born in 1916-1935 residing in the Petrogradskii District by the 1974 voting lists</td>
</tr>
<tr>
<td></td>
<td>Leningrad</td>
<td>Men born in 1916-1935 residing in the Petrogradskii District by the 1974 voting lists</td>
</tr>
</tbody>
</table>
ing preparation of an isopropanol extract of plasma and subsequent treatment with a zeolite mixture to remove phospholipids, glucose, and bilirubin and then simultaneous determination of cholesterol and triglyceride by use of an AAII Technicon AutoAnalyzer. Blood pressure was measured on the right arm, after the participant had been sitting for at least 5 min. Four blood pressure measurements were obtained, two with a standard mercury sphygmomanometer and two with a random zero sphygmomanometer. The average of two readings with a random zero sphygmomanometer was used in the present analysis. Systolic blood pressure was defined by the appearance of sound (Korotkoff’s first phase) and diastolic pressure by the disappearance of sound (fifth phase). Standing height, without shoes, was measured to the nearest 0.5 cm. Weight was measured to the nearest 0.1 kg in ordinary street clothes without heavy outer garments. The body mass index (Quetelet index) was calculated by use of the formula [weight (kg)/height\(^2\) (cm)] \times 1000.

Resting electrocardiograms were obtained to detect evidence of CAD and previous myocardial infarction. Standard 12-lead ECGs were performed in both countries with participants comfortably recumbent. They were recorded on analog magnetic tape (Hewlett-Packard Model 1516A; Palo Alto, CA) in the U.S. clinics and on a four-channel ink jet recorder (Mingograf Model 3400; Seimens-Elema, Sweden) at a sensitivity of 1.0 cm/mV and paper speed of 50 mm/sec in the two U.S.S.R. clinics. Both recording modes had frequency responses in excess of 0.05 to 125 Hz. Limb leads were recorded with the Mason-Likar torso modification suitable for exercise testing.\(^{24}\) The arm leads were attached in the lateral aspects of the infracavicular fossa to minimize distortion of lead I recordings.

Before the exercise test, a physician obtained a medical history and physical examination to determine whether subjects were eligible for the treadmill test or were to be rescheduled or excluded. Reasons for exclusions were recorded. The treadmill exercise test procedure was the Bruce protocol as modified by Sheffield and Roitman.\(^{25}\) These were seven 3 min stages; the speed ranged from 1.7 mph in stage 1 to 6.0 mph in stage VII and the slope ranged from 10% to 22%. Exercise continued from one stage into the next without interruption until subjects reached 85% to 90% of their age- and physical activity-adjusted, predicted maximal heart rate unless stopped due to exhaustion or medical contraindications.\(^{26}\) Reasons for terminating the test other than reaching target heart rate were recorded. They included fatigue or dyspnea, chest pain consistent with angina pectoris, leg pain consistent with peripheral vascular disease, inappropriate blood pressure response (hypotension or hypertension), dizziness, ECG abnormalities (selected ventricular or supraventricular arrhythmias or 1 mm ST segment depression), and technical problems. The ECG was continuously monitored during the test and recovery, and six leads (V\(_A\), V\(_S\), V\(_D\), X, Y, and Z) were recorded on paper at the end of each 3 min stage of exercise, immediately after exercise, and at minutes 2, 4, and 6 of recovery. The Frank leads X, Y, and Z were not used for the present analysis. Arterial blood pressures were also recorded at rest at these same times by the cuff method.

**Analysis of ECG recordings.** ECG recordings from both countries were sent to the LRC Program Central Electrocardiographic Laboratory at the University of Alabama for central coding. ECGs that had been recorded on magnetic tape were digitized and reproduced on paper by a computer program before visual coding of significant Q, ST, or T wave abnormalities (Minnesota code, see Appendix 1). All ECGs were independently analyzed by two coders; the U.S. recordings were additionally analyzed by a computer program.\(^{25}\) The results were reviewed by a senior coder who corrected any apparent errors. Subtle or equivocal disparities between codings were adjudicated by the laboratory director. The verified ECG codings were transferred to magnetic tape and sent to the data coordinating center at the University of North Carolina and to the originating clinics.

Resting ECGs were considered to have major or minor Q wave abnormalities as categorized by the Minnesota code (tabulated in Appendix 1 and ref. 7). Subjects were considered to have “major ischemia” if either major T or major ST abnormalities were present. Subjects were considered to have “minor ischemia” if either minor T, minor ST, or Q wave abnormalities were present. Subjects who were taking digitalis or who had resting ECGs of inadequate technical quality were excluded from this analysis (53 in U.S. and eight in U.S.S.R.).

EGCs characteristic of left ventricular hypertrophy (LVH, see Appendix 1) were analyzed only for Q wave abnormalities because ST or T abnormalities in subjects with LVH may not necessarily be indicative of underlying CAD. Hypertension (the most frequent cause of LVH) was more prevalent in the U.S.S.R. sample than in the U.S. sample.\(^{27}\) One subject in the U.S. and eight subjects in the U.S.S.R. had ECGs characteristic of LVH.

Results of the graded exercise test were considered positive if the visually coded ST depression was 1 mm or greater. A treadmill test was considered nondiagnostic if the test was not ECG positive and if the person failed to reach a target heart rate calculated from 180 – (0.66 \times age) or terminated the test because of leg pain, arrhythmias, or hypertension.

**Rose questionnaire.** Chest pain was assessed with the Rose questionnaire administered by a trained interviewer at visit 2 (see Appendix 1).

**Statistical methods.** This analysis involves the 15% random sample of visit 1 participants who returned for the visit 2 examination. Visit 2 had a 90% response rate in both countries. For each country, estimated prevalence rates were computed for selected ECG abnormalities and angina in two age groups (40 to 49 and 50 to 59). For each abnormality, age-adjusted prevalence rates in the two countries were compared by Mantel-Haenszel (MH)\(^{28}\) and stratified chi-square.\(^{29}\) For the ith (i = 1, 2) age group, the MH chi-square statistic, \(\chi^2_{\text{MH}}\), was computed and then

\[
\chi^2_{\text{Total}} = \sum_{i=1}^{2} \chi^2_{i}
\]

was obtained. Also, the MH statistic over all ages (denoted as \(\chi^2_{\text{Comb}}\)) was calculated and used in testing for significant differences between the two age-adjusted prevalence rates. Finally, the statistic \(\chi^2_{\text{Diff}} = \chi^2_{\text{Total}} - \chi^2_{\text{Comb}}\) was used for testing whether there was a crossover effect over the age groups.\(^{29}\)

Means and standard errors of selected cardiovascular risk factors were computed for subjects with resting and stress ECG abnormalities or angina and for subjects free of any tested abnormality. Mean values of five risk factors (HDL cholesterol, LDL cholesterol, triglycerides, systolic blood pressure, and Quetelet index) in each abnormality group were compared with the corresponding means of participants with no detected abnormalities. Differences were tested for statistical significance (t test). Comparisons were restricted to these five risk factors to reduce the probability of making type I errors with repeated t tests. In addition, means of the five risk factors were similarly tested for between-country differences. Moreover, to control for multiple comparisons, two sets of two-way analysis of variance models were fitted, one set comparing the group with any evidence of cardiovascular ischemic disease with the no-abnormality group, a second set comparing the angina group with the no-abnormality group. The models were fitted on the same five risk factors as were used in the t tests and contained model terms for country, an indicator for the abnormality group of compar-
ison, and their interaction. If the interaction term was non-
significant, models were fitted without this term; the significance
level was set at .01 for hypothesis testing.

Results
Age-stratified prevalence rates and frequencies of
resting and stress ECG abnormalities and angina are
listed in table 2. Statified \( \chi^2 \) analysis indicated that
there was no statistically significant difference in pre-
valence of major Q waves (infarction) between the two
countries, possibly because of the small proportion of
Q waves. The same was found for the prevalence of
major ischemia. Major T and Major ST abnormalities
were more prevalent in older age groups in both coun-
tries. The prevalence of minor ischemia was signific-
antly higher in the U.S. sample, but no statistically
significant differences were detected when minor isch-
emia subcategories were analyzed, again possibly
related to the small proportion of abnormalities.

By the Rose questionnaire, the estimated prevalence
of angina in the U.S. sample was less than 50% of that
in the U.S.S.R. sample (p < .01). The prevalence of

TABLE 2
Age-specific prevalence rates (per 1000 population) of ECG abnor-
malities in men, ages 40–59, U.S. and U.S.S.R. samples

|---------------------|--------------|--------------|------------------|------------------|
| Resting ECG abnorm-
|alities              |              |              |                  |                  |
| Population at risk  | 524          | 473          | 559              | 399              |
| MI or ischemia      | 22           | 42.0         | 23               | 48.6             |
| Major Q             | 4            | 7.6          | 5                | 10.6             |
| Major ischemia      | 3            | 5.7          | 7                | 14.8             |
| Major T             | 3            | 3.8          | 2                | 6.3              |
| Major ST            | 1            | 1.9          | 1                | 3.6              |
| Minor ischemia      | 15           | 28.6         | 11               | 23.3             |
| Minor T             | 6            | 11.5         | 7                | 14.8             |
| Minor ST            | 1            | 1.9          | 1                | 3.6              |
| Minor Q             | 9            | 17.2         | 5                | 10.6             |
| Stress ECG abnorm-
|alities              |              |              |                  |                  |
| Population at risk  | 508          | 429          | 493              | 294              |
| GXT                 | 12           | 23.6         | 35               | 81.6             |
| Rose questionnaire   |              |              |                  |                  |
| Population at risk  | 524          | 473          | 559              | 399              |
| Angina              | 7            | 13.4         | 21               | 44.4             |

MI = myocardial infarction; GXT = graded exercise test.

Subjects with major Q abnormalities are not included in the major
ischemia category regardless of whether they had major T or major ST
abnormalities.

Subcategories of major and minor ischemia may not sum to total in
each column due to double counting and exclusions noted in the defini-
tions (see Appendix 1).

GXT results were missing for 60 subjects in the U.S. and 171
subjects in the U.S.S.R.

TABLE 3
Number and percentage of subjects excluded from graded exercise
test, a ages 40–59, U.S. and U.S.S.R. samples

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>42</td>
<td>100.0</td>
<td>161</td>
<td>100.0</td>
</tr>
<tr>
<td>Aortic stenosis</td>
<td>2</td>
<td>4.8</td>
<td>1</td>
<td>0.6</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>1</td>
<td>2.4</td>
<td>8</td>
<td>5.0</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>8</td>
<td>19.0</td>
<td>31</td>
<td>19.3</td>
</tr>
<tr>
<td>R or T type PVCs</td>
<td>1</td>
<td>2.4</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>Ventricular tachycardia</td>
<td>2</td>
<td>4.8</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>Asystolic focus</td>
<td>0</td>
<td>0.0</td>
<td>1</td>
<td>0.6</td>
</tr>
<tr>
<td>Atrial flutter</td>
<td>0</td>
<td>0.0</td>
<td>2</td>
<td>1.2</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>0</td>
<td>0.0</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>Congenital heart disease</td>
<td>1</td>
<td>2.4</td>
<td>1</td>
<td>0.6</td>
</tr>
<tr>
<td>Scheduling problems</td>
<td>7</td>
<td>16.7</td>
<td>7</td>
<td>4.3</td>
</tr>
<tr>
<td>Possible active or subactive MI b</td>
<td>0</td>
<td>0.0</td>
<td>4</td>
<td>2.5</td>
</tr>
<tr>
<td>Other reasons b</td>
<td>24</td>
<td>57.1</td>
<td>115</td>
<td>71.4</td>
</tr>
</tbody>
</table>

PVCs = premature ventricular contractions; other abbreviations as in
table 2.
aNumber of subjects and percentages do not add to total because
some individuals had multiple reasons for exclusion.
bTranslation of data collection forms between the two countries ac-
counted for slightly differing reasons for exclusion between the two
countries.

angina in each country’s sample was much greater in
the 50 to 59 year age group than in the 40 to 49 year age
group.

Analysis of the graded exercise test abnormalities
did not reveal any trend suggesting differences in pre-
valence of CAD between the two samples, but the true
prevalence of CAD in the U.S.S.R. sample is probably
underestimated because of a higher proportion of men
excluded from the exercise test for various reasons.
Thus a group of individuals with a high probability of
ischemic heart disease was not given exercise tests. As
shown in table 3, there were 161 exclusions (17%) in
the U.S.S.R. and 42 exclusions (4%) in the U.S. The
most frequent reason for exclusion in both samples was
elevated blood pressure. After accounting for subjects
reaching their target heart rate in the U.S.S.R., subjects
terminating the exercise test did so for a variety of
reasons including fatigue (10%), dyspnea (9%), leg
pain (5%), chest pain (3%), ST changes (3%), cerebral
symptoms (3%), hypertension (2%), and refusal to
continue (2%). In the U.S. the most frequent reasons
for termination were fatigue (17%), dyspnea (10%),
leg pain (4%), ventricular tachycardia and other
arrhythmias (3%), ST changes (2%), and subject refus-
ing to continue (2%).

Table 4 provides means and standard errors of several
risk factors associated with ischemic cardiovascular
disease grouped according to myocardial infarction or
ischemia determined from the resting ECG, positive exercise test, and angina (by Rose questionnaire). They are also shown for the total group with one or more of these abnormalities and for individuals who had no abnormalities. Significance tests were performed for each country comparing an abnormality group with the no-abnormality group. Additional tests were done comparing corresponding groups across countries. To minimize the multiple comparisons problem, these tests involved the angina group, the total group with one or more abnormalities, and the group with no abnormalities. Tests were restricted to five risk factors (HDL cholesterol, LDL cholesterol, triglycerides, Quetelet index, and systolic blood pressure) and the results are shown in the boxed section of table 4.

In comparing abnormality and no-abnormality groups, some differences were evident. For the angina group, only the means for HDL cholesterol in the U.S. and systolic blood pressure in the U.S.S.R. were significantly different from means of men in the no-abnormality group. HDL cholesterol was lower for the angina group in the U.S.; systolic blood pressure was higher in the U.S.S.R. For men with one or more abnormalities, the means for HDL cholesterol in the U.S. and systolic blood pressure in both countries were significantly different from those in the no-abnormality group. Men with abnormalities had lower HDL cholesterol and higher systolic blood pressure. Although not tested statistically, men with abnormalities had higher mean diastolic blood pressure and total cholesterol than men with no abnormalities. Except for U.S.S.R. men in the group with graded exercise test abnormalities, percentages of smokers were lower in persons with abnormalities than in those without.

| TABLE 4 | Means and standard errors of ischemic cardiovascular risk factors by type of abnormality, with selected significance tests, in men ages 40–59, U.S. and U.S.S.R. samples |
|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|
| Risk factor by country          | MI or ischemia                  | GXT                             | Angina                          | MI, ischemia                    | No abnormality                  |
| Number of cases                 | X| SE | X| SE | X| SE | X| SE | X| SE | X| SE |
| U.S.                            | 45| 46 | 28 | 107 | 886 |
| U.S.S.R.                        | 38| 32 | 62 | 111 | 840 |
| HDL cholesterol (mg/dl)         | U.S. | 43.0 | 1.6 | 43.6 | 1.5 | 39.0^p | 1.7 | 42.9^c | 1.0 | 45.7 | 0.4 |
| U.S.S.R.                        | 50.3 | 2.9 | 50.4 | 3.0 | 53.1^p | 2.7 | 51.8^f | 1.8 | 52.4 | 0.6 |
| LDL cholesterol (mg/dl)         | U.S. | 147.7 | 6.1 | 147.2 | 4.8 | 159.8 | 8.1 | 149.6 | 3.6 | 143.2 | 1.1 |
| U.S.S.R.                        | 153.8 | 6.0 | 156.6 | 8.2 | 152.9 | 4.3 | 154.8 | 3.7 | 147.1^f | 1.3 |
| Triglycerides (mg/dl)           | U.S. | 180.1 | 21.1 | 155.9 | 13.8 | 166.1 | 18.1 | 160.7 | 10.5 | 143.4 | 3.8 |
| U.S.S.R.                        | 121.8 | 8.8 | 133.4 | 10.6 | 129.9 | 10.0 | 128.5^f | 6.7 | 122.4 | 2.9 |
| Quetelet index (kg/cm^2)/100    | U.S. | 2.73 | 0.06 | 2.68 | 0.04 | 2.67 | 0.09 | 2.70 | 0.04 | 2.63 | 0.01 |
| U.S.S.R.                        | 2.75 | 0.07 | 2.63 | 0.05 | 2.64 | 0.04 | 2.67 | 0.03 | 2.58^f | 0.01 |
| Systolic BP (mm Hg)             | U.S. | 130.7 | 2.9 | 133.5 | 3.0 | 132.5 | 4.8 | 131.3^p | 2.0 | 125.7 | 0.6 |
| U.S.S.R.                        | 148.3 | 4.3 | 143.6 | 4.3 | 142.2^e | 3.7 | 145.1^f | 2.7 | 134.3 | 0.7 |
| Total cholesterol (mg/dl)       | U.S. | 220.7 | 6.2 | 217.3 | 5.2 | 227.5 | 8.3 | 220.0 | 3.8 | 213.3 | 1.2 |
| U.S.S.R.                        | 227.1 | 5.1 | 232.8 | 8.8 | 231.2 | 4.5 | 231.3 | 3.6 | 222.5 | 1.4 |
| Diastolic BP (mm Hg)            | U.S. | 85.6 | 1.8 | 86.9 | 1.5 | 84.0 | 3.1 | 85.4 | 1.1 | 81.8 | 0.3 |
| U.S.S.R.                        | 96.1 | 2.5 | 90.1 | 2.1 | 93.0 | 1.9 | 93.2 | 1.4 | 89.6 | 0.4 |
| Percent smokers                 | U.S. | 24.4 | 23.4 | 32.1 | 26.9 | 39.4 |
| U.S.S.R.                        | 44.7 | 56.3 | 40.3 | 45.0 | 49.7 |

^aSignificance tests performed only on means in boxed area to decrease problem of multiple comparisons.

^bMI and ischemia determined by resting ECG.

^cP < .05; ^dP < .01, t test for difference between this mean and corresponding mean in "No abnormality" column.

^eP < .05; ^fP < .01, t test for difference between this mean and corresponding mean for U.S.
Between-country differences in means of the five risk factors tested for significance show that HDL cholesterol was higher in the U.S.S.R. in all three abnormality groups and these differences were statistically significant. Systolic blood pressure was also higher in the U.S.S.R. sample in all three groups and significantly different in all but the angina group. Mean triglycerides were lower in the U.S.S.R. sample in all three abnormality groups but significantly different only in the group with one or more abnormalities.

Analysis of variance models yielded similar results. In all models, the interaction term was considered nonsignificant, thus suggesting parallelism between the two countries for all the risk factors tested. In models where men with angina were compared with men free of ischemic cardiovascular disease, LDL cholesterol and systolic blood pressures were higher in the angina group, with country differences noted for HDL cholesterol (U.S.S.R. higher). For models comparing subjects with any evidence of ischemic cardiovascular disease to those with no evidence of disease, in addition to the same two risk factors, LDL cholesterol and systolic blood pressure, Quetelet index was also significant (higher in diseased subjects). Country differences were noted in all risk factors tested, with the U.S.S.R. having higher mean values of HDL cholesterol, LDL cholesterol, and systolic blood pressure and the U.S. having higher mean levels of triglycerides and Quetelet index.

Table 5 provides a cross-tabulation of resting ECG findings with Rose questionnaire angina responses. In both countries, a similar pattern of response was observed. Ischemic cardiovascular disease as evidenced by resting ECG is observed approximately three times as frequently in those with a positive Rose questionnaire angina response as in those with a negative outcome. Similarly, in those with resting ECG abnormalities, positive angina response is approximately three times as likely as in those subjects free of resting ECG ischemic responses.

### Discussion

Although not all differences in the prevalence of resting ECG changes are statistically significant, some trends can be observed in the table 2 data. Prevalence per 1000 population for major T, major ST, and major ischemia is higher in the U.S.S.R. sample than in the U.S. sample. In the U.S. sample, minor T and minor ST abnormalities are more prevalent in the 40 to 49 year age group and less prevalent in the 50 to 59 year age group as compared with the U.S.S.R. sample. This comparison indicates that there may be a higher prevalence of ischemia in the U.S.S.R. sample but a similar prevalence of earlier myocardial infarction in both samples. Individuals with ECG evidence for LVH were excluded from the ST and T analyses. However, the method used to diagnose LVH in the study had a low sensitivity and therefore we may have underestimated the true prevalence of LVH. Some of the ST and T wave changes may represent early stages of LVH and may not be signs of ischemia, especially in the U.S.S.R. with their higher blood pressure levels. On the other hand, the ST and T wave changes seen in early stages of LVH are also associated with an increased risk of future CAD in the same way as true ischemic changes. Both major T and major ST prevalence rates become significantly greater in the U.S.S.R. sample when subjects with LVH are included in the analysis (24.0 vs 11.0 per 1000, p < .05, and 13.6 vs 4.0 per 1000, p < .05). The prevalence of ST and T wave abnormalities and the prevalence of angina suggest a higher prevalence for CAD in the U.S.S.R., but ECG Q wave and treadmill abnormality prevalence rates do not show the same pattern.

Because of methodologic differences between the LRC Prevalence Study and other epidemiologic stud-

---

**TABLE 5**

<table>
<thead>
<tr>
<th>Rose questionnaire angina responses</th>
<th>U.S.</th>
<th>U.S.S.R.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MI or ischemia</td>
<td>No abnormality</td>
</tr>
<tr>
<td>Positive</td>
<td>4</td>
<td>24</td>
</tr>
<tr>
<td>Negative</td>
<td>41</td>
<td>927</td>
</tr>
<tr>
<td>Total</td>
<td>45</td>
<td>951</td>
</tr>
</tbody>
</table>

*One individual in the U.S. sample was missing the results of the Rose questionnaire and had no ECG abnormalities, thus the U.S. sample total is missing one subject from previous tables.

*Myocardial infarction indicated by major Q wave abnormalities.

Ischemia is indicated by major or minor T wave abnormalities, major or minor ST abnormalities, or minor Q wave abnormalities.
ies, comparisons of prevalence of ischemia between such studies should be interpreted cautiously. Nevertheless, a comparison of LRC findings with those reported for the European trial\textsuperscript{14} suggests that the prevalence of ischemia (indicated by resting ECG) in men 40 to 59 years old, in both the U.S. and U.S.S.R. samples, is low in relation to that in such countries as the United Kingdom, Belgium, and Italy and comparable to that in Poland and Spain.

The prevalence of angina by Rose questionnaire in the U.S.S.R. sample is more than twice that in the U.S. sample (64.7 vs 28.1 per 1000 population; \(p < .01\)), which suggests higher prevalence of ischemia in these U.S.S.R. participants. The higher prevalence of angina in the U.S.S.R. total sample is due primarily to the very high prevalence in the 50 to 59 year age group. This group also had a high prevalence of major and minor Q wave abnormalities, which provides additional evidence for the presence of CAD. Exact reasons for the apparent higher prevalence of angina in the U.S.S.R. sample compared with the U.S. sample are unknown. However, there are probably several reasons, including higher prevalence of hypertension, selection of men from only large industrial centers, and problems of application of the Rose questionnaire in different cultures.\textsuperscript{30, 31}

Validation of the ECG and angina criteria as evidence for CAD in this study is indicated by cross-tabulation of ECG findings with the Rose questionnaire angina responses in table 5. As noted earlier, among those with a positive angina response from either country, myocardial infarction or ischemic ECG responses were found about three times more frequently than among those with a negative angina response. Within each sample, the percentage of participants with ECG abnormalities who had angina was three times the proportion in those with no ECG abnormality. This suggests that both ECG and angina criteria are correlated with the presence of coronary heart disease. True misclassification rates are not known, since this validation is indirect and incomplete.

The true incidence of CAD is probably higher than indicated by the end points used in this study, in part related to the observation that both angina\textsuperscript{32, 33} and ECG findings\textsuperscript{34} may be transient and therefore may be absent during the study. In spite of these concerns, the estimated prevalence of angina in the U.S. sample is within the range of reported estimates for this age group in another study\textsuperscript{14} in which angina estimates ranged from 23 per 1000 population in Spain to 51 per 1000 population in Poland, with an average estimate of 43 for the five countries involved in that study. Angina prevalence in a Polish study was 36 per 1000 in the 40 to 44 year age group and 77 per 1000 in the 55 to 59 year age group.\textsuperscript{35} This dramatic increase in the older age group is similar in magnitude to the increase observed in the U.S.S.R. LRC sample.

Mean values of selected risk factors for different categories of ECG abnormalities (table 4) generally conform to what one would expect. However, mean HDL cholesterol levels in the U.S.S.R. sample are similar in people with or without any evidence for CAD, whereas the HDL mean for the group with no abnormality in the U.S. sample is considerably higher (\(p < .05\)). The U.S. sample follows the expected trend of lower mean HDL cholesterol levels in participants with ECG abnormalities or angina. Triglyceride means are considerably higher in the U.S. sample. Systolic blood pressure in the U.S.S.R. sample was higher. These differences suggest an important interaction between these risk factors and the development of CAD. Systolic blood pressure has been found to be more positively associated with ECG abnormalities than diastolic blood pressure.\textsuperscript{36} Also for the U.S. sample, there was a smaller percentage of smokers with exercise test abnormalities than in the group with one or more abnormalities. Although not seen in the U.S.S.R. sample, similar findings have been discovered by other investigators in that ST depressions during exercise have been found less frequently in smokers than nonsmokers.\textsuperscript{36–40}

In summary, little difference in the prevalence of ECG changes was observed between these U.S. and U.S.S.R. samples in this study. The prevalence of major ECG Q waves in both countries was lower or comparable to figures reported in other studies.\textsuperscript{14, 35, 36} Major ischemic changes as indicated by resting ECG appear to be more prevalent in the U.S.S.R. sample than in the U.S. sample. Minor findings, which are less specific indicators of ischemia, were more prevalent in the U.S. sample. ECG abnormalities were more prevalent in the older age group of both samples. Stress-induced abnormalities indicated no difference in CAD prevalence, but more subjects with a history compatible with CAD were excluded from the U.S.S.R. sample. Results of chest pain questionnaires are suggestive of a higher prevalence of ischemia in the U.S.S.R. sample.

We gratefully acknowledge the secretarial assistance of Ernestine Bland.

\textbf{Appendix 1}

\textbf{Resting ECG changes}

\textit{Minor Q waves}

Minnesota codes 1-2-8 or 1-3-1 through 1-3-6

\textit{Major Q waves}

Minnesota codes 1-1-1 through 1-1-7 or 1-2-1 through 1-2-7
PATHOPHYSIOLOGY AND NATURAL HISTORY—ISCHEMIC HEART DISEASE

Minor T waves
Minnesota codes 5-3, no LVH

Major T waves
Minnesota codes 5-1 or 5-2, no LVH

Minor ST depression
Minnesota codes 4-3, no LVH

Major ST depression
Minnesota codes 4-1 or 4-2, no LVH

Myocardial infarction

Major Q

Major ischemia
Major ST or major T; no major Q

Minor ischemia
Minor Q or minor T or minor ST; no major Q or major ischemia

LVH
R wave (3.1 or 3.3) and major or minor ST depression or major or minor T wave

Clinical symptoms
Rose questionnaire angina
Positive response to following questions on the LRC Visit 2 Questionnaire — 31a, 32 or 33, 34, 35, 36, 37a or 37b, or (37c and 37d) conforms to WHO criteria.7.20
Q31. “Have you ever had any pain or discomfort in your chest?” “Yes”
Q32. “Do you get it when you walk uphill or hurry?” “Yes”
Q33. “Do you get it when you walk at an ordinary pace on the level?” “Yes”
Q34. “What do you do if you get it while you are walking?” “Stop or slow down”
Q35. “If you stand still, what happens to it?” “Relieved”
Q36. “How soon?” “Ten minutes or less”
Q37a,b,c,d. “Will you show me where it was?” “Upper sternum,” “Lower sternum,” “Left anterior chest,” “Left arm”

Appendix 2

U.S.-U.S.R. Steering Committee

Working Group

Lipid Research Clinics Directors

Project Officer, North American Lipid Research Clinics

Central Agency Directors

Epidemiology Committee

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