

Cardiovascular Risk Factors and Mortality. Long-Term Follow-up (up to 20 years) in a Preventive Program Carried out by Occupational Medicine

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Objective

The decrease in mortality due to cardiovascular diseases (CVD) has been achieved in the United States and the same decrease has been happening in developing countries, thanks to favorable changes in lifestyle and risk factors. Despite such consideration, the volume of information available on the distribution and behavior of that type of disease and its risk factors in Brazil is still little.

Methods

The assessment of changes in total cholesterol (TC), levels of blood pressure (BP), body mass index (BMI) and smoking was carried out, besides the occurrence of fatal (F) and non-fatal (NF) cardiovascular events, under dietary and behavioral intervention and long-term follow-up (up to 20 years) in a closed group, consisting of 621 electric power company workers of both sexes, with average age of 29.1 ± 7.1 years old, varying from 15 to 59 years old. Actuarial curves were obtained to analyze the F and NF cardiovascular events.

Results

The TC mean showed significant reduction due to dietary guidance. The smoking habit decreased significantly with behavioral changes. The mean of the BPs decreased significantly with a better detection and hygienic measures, and the adherence by definite hypertensive people to the treatment showed an index of 56.6%. On the other hand, the BMI showed an expressive and gradual increase. The probability for the individuals to remain free of any cardiovascular event was of 98.1%, whereas for the fatal events, it was 99.2%.

Conclusion

Those results prove that initiatives directed towards the prevention must be priorities, aiming at modifying the morbimortality rates of CVD.

Key words

cardiovascular risk, preventive medicine, occupational medicine

The decrease of mortality due to cardiovascular diseases (CVD) has been achieved in the United States and the same decrease has been happening in developing countries¹⁻³. In Brazil, tendencies to the fall have also been identified, especially for CAD and cerebrovascular diseases (CbVD), in a well-documented manner for the metropolitan regions, notably Belém, Salvador and São Paulo, and, not so importantly, for the capitals of South Region, where the last rates have shown a tendency to stability⁴.

Despite such importance, the information available on the distribution and behavior of that kind of diseases and their risk factors in Brazil is still little: works by Costa⁵ and Achutti & Medeiros⁶, in Rio Grande do Sul, and those by Laurenti & Fonseca⁷, Ribeiro⁸ and Rego et al.⁹, in São Paulo, on hypertension and CVD.

So, having epidemiological assessments on such parameter at hand becomes imperative for the projections aiming at the decrease of cardiovascular mortality. Due to the importance of the theme, given to the growing participation of that mortality index in vital statistic and the scarcity of relevant studies carried out in Brazil, a clinical study on the risk factors of arteriosclerotic cardiovascular diseases was proposed, in the long-term follow-up (up to 20 years), in a closed population sample from the region of São José do Rio Preto (SP), with emphasis on the effect of preventive measures as dietary and behavioral guidance.

Methods

The study was developed in the region of São José do Rio Preto (northwest of the State of São Paulo), with 621 employees, of both sexes, of Companhia Paulista de Força e Luz, who worked in the cities of São José do Rio Preto, Mirassol, Barretos and Araçatuba, being the sample socioeconomically similar.

Those employees showed job stability, obligatoriness in being submitted to periodic, yearly or semestral medical examinations, and they were assessed in an ambulatory in the city of São José do Rio Preto, counting on a nursing assistant and a labor physician, who followed them up from January 1977 to December 1996. There the clinical examinations, measurements of weight, height and blood pressure, and venopuncture to determine total cholesterol, and other laboratorial exams were performed.

The age, at the beginning of the study, varied from 15 to 59 years old, with an average of 29.1 ± 7.1 years old, 580 were male, with average age of 29.4 ± 7.2 years old and 41 were female, with average age of 25.0 ± 5.2 years.

All participating employees showed a medical record, in which all health events occurred during the period were marked down.

The blood pressure measurements were taken in accordance to the techniques recommended by the World Health Organization¹⁰ (WHO – Hypertension Expert Committee, Geneva, 1978), with the use of aneroid sphygmomanometers duly calibrated with column of mercury equipment and periodically gauged.

The weight and height measurements were taken on a Filizola scale (with capacity for 150 kg and sensitivity of 100g), at the beginning of the yearly clinical appointment, with the employees free of heavy shoes and clothes, according to standardized techniques¹¹.

In blood samples collected after 12-hour fast the following biochemical exams were carried out: complete blood count, glucose, total cholesterol, HDL-cholesterol, LDL-cholesterol, triglycerides and creatinine. Total cholesterol was dosed using the colorimetric method of Liebermann-Burchard, in the period from 1977 to 1988, the modified colorimetric method of Huang, in the period between 1989 to 1993, and through the enzymatic system in a CHOD-PAP spectrophotometer, from 1994 to 1996.

The criterion of *Joint National Committee* (1997)¹² was used for the diagnosis of hypertension.

The body mass index (BMI) or Quetelet index, which is represented by the division of the weight (in kilograms) by the square of the height (in meters)¹³ was used. Concerning the total cholesterol (TC), the participants were divided in accordance to the criteria of III Consenso Brasileiro sobre Dyslipidemias – 3rd Brazilian Consensus on Dyslipidemias -, recommended by Sociedade Brasileira de Cardiologia - Brazilian Society of Cardiology - (Department of Atherosclerosis)¹⁴.

The employees who reported smoking daily, any number of cigarettes, were regarded as smokers.

Serum cholesterol, smoking, hypertension and BMI-assessed obesity were considered as risk factors for cardiovascular diseases.

Definite complications from CAD, sudden death, intermittent claudication, congestive heart failure, cerebrovascular accident and transitory ischemia were considered as cardiovascular events. Those diseases were diagnosed on clinical base, in conventional supplementary exams and, in fatal cases, in death certificate.

Information on the distribution of age and sex of the studied group is shown on table I, showing that most of individuals were within the age range between ≥ 20 and < 40 years old in the year 1977 (88%). The fact of the great prevalence of male sex is due to the type of professional activity of the individuals (electric power company workers of CPFL).

The aim of the intervention was of modifying the “risk factors” that, for some time, have been increasing their importance in the field of non-transmitted chronic diseases.

So, the employees were guided towards the elimination of

smoking habit, decrease and control of weight and the control of blood pressure in hypertensive. That process was carried out individually in the yearly periodic appointment and in group, with the help of talks and videos.

Concerning the borderline-high and high level TC, a standard diet was instituted aiming at reducing the ingestion of long chain fatty acids^{15,16}. Yearly or semi-annually, during the whole study, all individuals were guided by the physician of Occupational Medicine Ambulatory to replace saturated fats for polyunsaturated fatty acids, in addition to the increase of ingestion of vegetables and fiber-rich foods.

The feedback was always assessed in the yearly or semestral periodical exams or when necessary, which was facilitated by the commitment from CPFL with Preventive Medicine for being about a restricted group of employees. Astatine was prescribed in the cases that the TC ≥ 300 mg/dL.

The employee's database was done in MSExcel and the analyses through Solo Statistical System (Version 2.0) software, with which the means and standard deviation and the matching t-test were calculated for each variable in the study. The comparisons of two proportions were carried out with Primer Software.

Actuarial curves were obtained to analyze the appearance of cardiovascular events and deaths in the time of the study. The actuarial method, among the methods of tardive analysis of results, is the most suitable as it gathers patients with different follow-up times, uses information from all patients, regardless of time distribution, and it can be used to estimate the “probability of being free” of many events, as well as allows for the comparison of results from other populations.

Significant values of $p < 0.05$ were considered and the confidence intervals (CI) 95% were calculated.

Results

The three-year variations of average levels \pm standard deviation of total cholesterol (TC) are shown on figure 1, in which there is an increase in year 1983 and then a gradual decrease until year 1995. When we compared the values found in 1977 with those found in 1995, there was a non-significant decrease of 1.5 mg/dL ($p = 0.334$). If the comparison is of 1983 with 1995, there was a significant reduction ($p < 0.01$ CI 95% 9.67 to 16.48) of 13.2 mg/dL (6.2%). In the comparison regarding sex, we found similar results.

When we assess the three-year variations of serum cholesterol in accordance to the 3rd Brazilian Consensus on Dyslipidemias, we find the number of individuals with desirable level, significantly increasing from 295 (47.5%) to 348 (57.1%) ($P < 0.01$), with

Age	Male	Female	Total
<20 years	21	2	23
=20 <30 years	300	34	334
=30 <40 years	209	4	213
=40 <50 years	45	1	46
=50 <60 years	5	-	5
Total	580	41	621

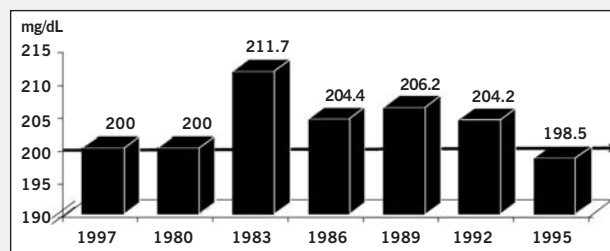


Fig. 1 - Three-year variation of average levels of serum cholesterol in individuals followed-up in the period from 1977 to 1996.



those with high level also decreasing significantly from 127 (20.5%) to 83 (13.6%) ($P < 0.01$) and the borderline-high group not showing significant changes when the years 1977 and 1995 ($p = 0.335$) are compared (fig. 2).

The changes in the prevalence of smoking habit, after a 20-year follow-up, is shown on table II, in which the number of smokers significantly decreased from 338 (54%) to 181 (30%) ($p < 0.01$).

The distribution of mean \pm SD of body mass index (BMI) is in figure 3, which verifies a gradual and significant increase when comparing 1977 to 1995 ($p < 0.01$), with the passage from 23.3 ± 3.2 kg/m² to 27.3 ± 3.9 kg/m².

The mean and standard deviation of systolic and diastolic blood pressures are shown on table III, in which the years 1977 and 1996 are compared. A significant decrease from 125.8 ± 11.7 mmHg to 124.0 ± 12.0 mmHg in systolic pressure ($p < 0.01$) is verified, as well as a significant increase from 76.9 ± 6.8 mmHg to 80.7 ± 7.0 mmHg ($p < 0.01$) in the diastolic pressure (tab. III).

The mean and standard deviation of systolic and diastolic pressures of definite hypertensive individuals, with and without treatment, at the end of the study in 1996 are on table IV. The systolic

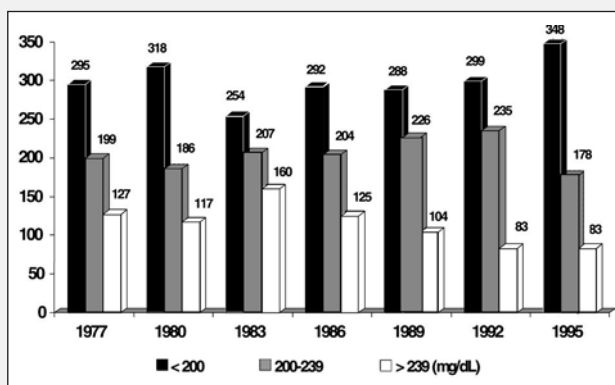


Fig. 2 - Three-year variation of the prevalence of serum cholesterol in accordance to the 3rd Brazilian Consensus on Dyslipidemias, in individuals followed-up in the period from 1977 to 1996.

Habit	Year 1977		Year 1996	
	n	%	n	%
Smokers	338	54	181*	30
Non-Smokers	283	46	428	70
Total	621	100	609	100

* $P < 0.01$ in relation to 1977.

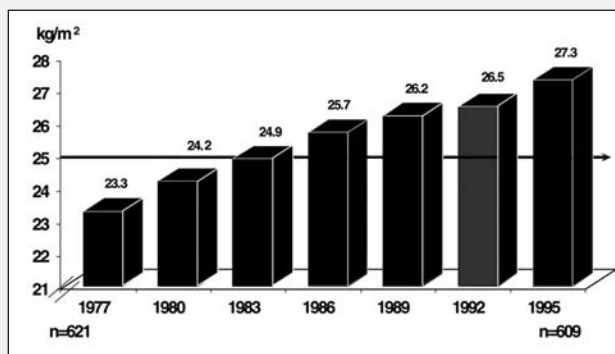


Fig. 3 - Average three-year distribution of body mass index, in individuals followed-up in the period from 1977 to 1996.

Table III - Mean and standard deviation of systolic and diastolic blood pressure in individuals after a 20-year follow-up (1977-1996)

Blood pressure (mmHg)	Year 1977	Year 1996
Systolic	125.8 ± 11.8	$124.0 \pm 12.0^*$
Diastolic	76.9 ± 6.8	$80.7 \pm 7.0^*$
Number	621	609

* $P < 0.01$ in relation to 1977.

Table IV - Mean and standard deviation of systolic and diastolic blood pressure (mmHg) of definite hypertensive individuals**, with and without treatment, at the end of the study in 1996

Blood Pressure	Without treatment (n=43)	With treatment (n=56)	p
Systolic	150.2 ± 12.8	131.8 ± 9.2	*
Diastolic	97.0 ± 6.6	85.0 ± 5.6	*

* $P < 0.01$: significant difference; ** SBP ≥ 40 and/or DBP 90 or being treated with medication.

and diastolic pressure levels were significantly lower in those treated individuals ($p < 0.01$ CI 95% 14.1 to 22.8 and $p < 0.01$ CI 95% 9.6 to 14.4, respectively).

The occurrence of fatal and non-fatal cardiovascular events and of deaths non-related to CVDs, for the period from 1977 to 1996, is shown on table V. Twelve events occurred, which correspond to an incidence of 0.97 event per 1,000 individuals per year. For the 5 fatal and 7 non-fatal events, we have an incidence of 0.40 and 0.56 events per 1,000 individuals per year, respectively.

The probability of being free of any non-fatal and fatal cardiovascular event, in the period of 20 years (1977 to 1996), according to actuarial curve (fig. 4) was 98.1% and 99.2%, respectively.

Discussion

Anatomopathological data and data from experimental, clinical and epidemiological investigations show the relation among dyslipidemias, especially the hypercholesterolemia, and the coronary artery disease.

Results from those investigations allowed for verifying that the reduction of cholesterolemia is able to decrease significantly the clinical events and the deaths resulting from CAD, as well as cardiovascular mortality¹⁷⁻²⁷.

Up to 20 years of follow-up (1977-1996), it was possible to demonstrate a non-significant decrease of 1.5 mg/dL for the plasmatc TC of the whole group. The three-year variations of TC levels showed an increase of the average values in the year 1983. The

Table V - Occurrence of fatal and non-fatal cardiovascular events and non-related deaths in individuals followed-up in the period from 1977 to 1996

Events	1977-1996
Cardiovascular diseases	
Fatal	5
Non-fatal	7
Non-related deaths	7
Total	19

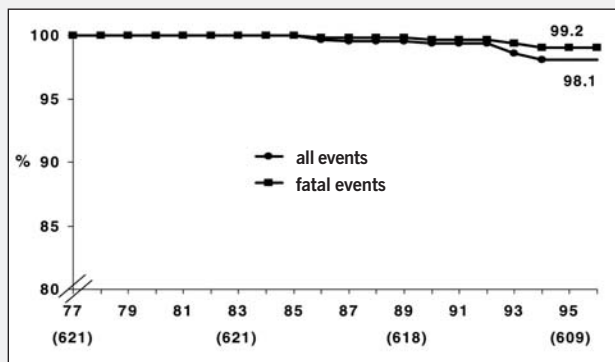


Fig. 4 - Actuarial curve of individuals free of any cardiovascular event and free of fatal cardiovascular events in the 20-year follow-up.

management to reduce hypercholesterolemia occurred that year was the dietary change to all individuals who showed TC ≥ 200 mg/dL and use of statins in those cases that TC ≥ 300 mg/dL. The results showed a significant decrease of the values of TC (13.2 mg/dL) when compared to those in the years 1983 and 1995.

When the three-year variations of serum TC were assessed, according to the 3rd Brazilian Consensus on Dyslipidemias, a significant increase of the number of individuals with desired levels was found and also a significant decrease of the number of individuals with high levels, when the years of 1977 and 1995 are compared.

Those results are similar to those from several studies on primary intervention that used different alimentary changes, but basically used the reduction of ingestion of foods rich in cholesterol and saturated fatty acids, and an increase of those with unsaturated fatty acids and complex carbon hydrates.

Smoking is one of the most important risk factors cardiovascular diseases and also neoplasias, chronic bronchitis and emphysema. Its high prevalence victimizes many individuals, especially due to atherosclerotic cardiovascular disease. It is regarded by the World Health Organization (WHO) and by the Department of Health of the United States as the most important avoidable risk factor of morbidity and mortality. Despite many scientific evidences pointing out to smoking malignancies, approximately a fifth of the world population consist of smokers. In Brazil, it is estimated that smoking is responsible for about 100 thousand deaths per year.

Intervention on smoking as objective of primary and secondary prevention of cardiovascular diseases allow for an important reduction of morbimortality, determining a better and greater survival in individuals who stop smoking, of both sexes and in any age range²⁸⁻³⁵.

In the present study, with the help of different methods of smoking interruption, such as behavioral changes (talks, videos, periodical exams), pharmacological preparations of nicotine, acupuncture, etc., it was possible to obtain satisfactory results, in which the number of smokers decreased from 338 to 181 (24%) in the whole group.

The results reached were comparable to those in the great international clinical studies of actuation on main risk factors³⁶⁻⁴⁰.

A longitudinal study, performed in the city of Framingham⁴¹, showed the association of obesity with morbimortality due to cardiovascular disease in both sexes and different age ranges. The coexistence of disorders as dyslipidemia, diabetes mellitus and hypertension, made impossible to identify the obesity as an

isolated risk factor for cardiovascular disease. Only after 26 years of assessment and a new analysis is that obesity was defined as an independent risk factor for cardiovascular disease⁴², despite that relation has not always been confirmed⁴³.

In the present study, the body mass index increased gradually and significantly when the years 1977 and 1995 are compared, with values of 23.3 ± 3.2 and 27.3 ± 3.4 kg/m², respectively. That number was also certified by Lotufo⁴⁴.

The certification that obesity was increasing assigned preventive measures for its reduction during the follow-up of the group, with nutritional guidance and incentive to regular physical exercises for a short period (approximately 1 year), but that did not have the desired effect, despite the efforts.

Hypertension is one of the most important risk factors for CVDs, as many epidemiological studies show but it is also, potentially, the one with the easiest approach, because its prevalence among adults is about 20%, there are efficient pharmacological and non-pharmacological therapeutics in its control, its initial identification and treatment require few technological and work-up resources, and finally the current treatment schemes have few side effects, with good tolerability.

The prevalence of hypertension for the period between 1977 and 1996 was approximately 16%. It has been estimated that approximately 1 out of 5 adults have hypertension in the United States, which means, 20%⁴⁵. In Brazil, many studies demonstrate that hypertension has variable prevalence.

The mean and the standard deviation of systolic pressure in this study showed a significant decrease from 125.8 ± 11.7 to 124.0 ± 12.0 mmHg, whereas the diastolic pressure showed a significant increase from 76.9 ± 6.8 to 80.7 ± 7.0 mmHg. A better detection and a better control of hypertension, with the help from periodical (yearly, semestral) exams, decreased the average level of systolic pressure of those individuals and reduced its prevalence.

Lolio and Laurenti⁴⁶, in 1986, showed results from the decrease of tendencies of mortality due to CAD from 1976, in the city of São Paulo. The same was observed for the cerebrovascular disease, in which the decrease was already noticed since the early 1970s. Lolio and Laurenti⁴⁶, Lotufo⁴⁷, Lotufo and Lolio⁴⁸, Lolio et al.^{49,50} showed that the mortality due to CAD and cerebrovascular disease is decreasing in the State of São Paulo in years 1980-1989. Other Brazilian capitals also showed a decrease in mortality due to CVD⁴. The systolic and diastolic pressure levels were significantly lower in those treated individuals. The adherence to the use of medications was considerable, as the company contributed with 30% from their cost.

In our study, during the observation period, 12 individuals died, being 5 of them concerning to CVDs and 7 non-related to, without having significant difference among them. Among the ones due to CVDs, 2 were due to coronary events and 3 due to cerebrovascular diseases.

The probability of being free of all cardiovascular events, according to the actuarial curve, was 98.1% and the fatal events due to CVD, was 99.2%.

This work could be achieved because we used epidemiological knowledge that evolved after the postulate of (1970)⁵¹ and the lessons the study of Framingham have supplied us with in the different stages of its publishing. In Brazil there are difficulties for



comparisons with other studies due to the characteristics of this research, sample with same socioeconomic standard, for being about a closed group of employees and especially for the involvement from CPFL in relation to the importance of Preventive Medicine.

So, the importance of health services in the workplace is highlighted, not only to identify risk groups, but especially for the performance of activities of education on health that aim at modifying life habits or styles that give rise to the whole community.

With the long-term (20 years) intervention (on the main risk factors for cardiovascular diseases) of a closed group consisted of 621 electric power company workers, we verify as follows: a) The average of total serum cholesterol showed a significant

decrease by the effect of dietary guidance, especially from the year of the sixth year of follow-up, increasing the number of individuals with desirable level and decreasing the number of those with high level. Smoking also decreased significantly, with behavioral changes. The average of systolic blood pressure significantly decreased with a better detection and hygienic measured taken during the periodical exams. The use of medications reduced significantly the systolic and diastolic pressure levels. The body mass index showed a significant and gradual increase. b) Regarding the cardiovascular events, the probability of being free of any event was 98.1% and the probability of being free of fatal events was 99.2%.

References

- Havlik RJ, Feinleib M. (Ed.). Proceeding of the conference on the decline in coronary heart disease mortality. Bethesda: National Institute of Health; 1979 (NIH publ. 79-1610).
- Uemura K, Pisa Z. Trends in cardiovascular disease mortality in industrialized countries since 1950. *World Health Stat Q* 1988; 41: 155-78.
- Lolio CA, Souza JMP, Laurenti R. Decline in cardiovascular disease, mortality in the city of S. Paulo, Brazil, 1970 to 1983. *Rev Saúde Pública* 1990; 20: 454-64.
- Lolio CA. Mortalidade por doença do aparelho circulatório em capitais de regiões metropolitanas do Brasil, 1979-1989. São Paulo: Faculdade de Saúde Pública. USP; 1994. 136 p. Tese (Livro Docência em Medicina Preventiva) - Faculdade de Saúde Pública. Universidade de São Paulo, 1994.
- Costa E. A cross-sectional survey of blood pressure in Rio Grande do Sul, Brazil. Londres: University of London; 1981. 132 p. Tese (Doutoramento em Medicina) - University of London, 1981.
- Achutti A, Medeiros AMB. Hipertensão arterial no Rio Grande do Sul. *Bol Saúde* 1985; 12: 6-54.
- Laurenti R, Fonseca LAM. A mortalidade por doenças cardiovasculares no município de São Paulo em um período de 30 anos (1940-1969). *Arq Bras Cardiol* 1976; 29: 85-8.
- Ribeiro MB, Ribeiro AB, Neto CS, et al. Hypertension and economic activities in São Paulo, Brazil. *Hypertension* 1981; 3: II-233-II-71.
- Rego RA, Berardo FA, Rodrigues SS, et al. Fatores de risco para doenças crônicas não-transmissíveis: inquérito domiciliar no município de São Paulo, SP (Brasil). Metodologia e resultados preliminares. *Rev Saúde Públ* 1990; 24: 277-85.
- Organização Mundial de Saúde. Genebra: Comitê de Expertos em Hypertension Arterial; 1978. Informe. Série de Informes Técnicos, 628.
- Rose GA. Métodos de encuesta sobre enfermedades cardiovasculares. 2. Ed. Ginebra: Organización Mundial de la Salud, 1982. (OMS - Série de Monografias, 56).
- Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure. The sixth report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of the High Blood Pressure. *Arch Intern Med* 1997; 157: 2413-46.
- National Institutes of Health Consensus Development Conference Statement. Health implications of obesity. *Ann Intern Med* 1985; 103: 1073-7.
- Sociedade Brasileira de Cardiologia - Departamento de Aterosclerose. III Diretrizes Brasileiras sobre Dislipidemias e Diretrizes de Prevenção da Aterosclerose. *Arq Bras Cardiol* 2001; 77(Supl III): 1-48.
- Keys A, Anderson JT, Grande F. Prediction of serum cholesterol responses of man to changes in fats in the diet. *Lancet* 1957; II: 959-66.
- Keys A, Anderson JT, Grande F. Serum cholesterol response to changes in the diet. IV. Particular saturated fatty acids in the diet. *Metabolism* 1985; 14: 776-86.
- Dayton S, Pearce ML, Hashimoto S, et al. A controlled clinical trial of a diet high in unsaturated fat in preventing complications of atherosclerosis. *Circulation* 1969; 40(suppl II): 1-63.
- Turpeinen O, Karvonen MJ, Pekkarinen M. Dietary prevention of coronary heart disease. The Finnish Mental Hospital Study. *Int J Epidemiol* 1979; 8: 99-118.
- Hjermann I, Velvebyre K, Holme I, et al. Effect of diet and smoking intervention on the incidence of coronary heart disease: report from the Oslo Study Group of a randomised trial in healthy men. *Lancet* 1981; 2: 1303-10.
- Multiple Risk Factor Intervention Trial Risk Factors. Changes and mortality results. *JAMA* 1982; 248: 1465-77.
- Multiple Risk Factor Intervention Trial Research Group. Mortality after 10 ½ years for hypertensive participants in the Multiple Risk Factor Intervention Trial. *Circulation* 1990; 82: 1616-28.
- Puska P, Salonen JT, Nissenen A, et al. Change in risk factors for coronary heart disease during 10 years of a community intervention programme (North Karelia Project). *Br Med J* 1983; 287: 1840-4.
- World Health Organization European Collaborative Group. European Collaborative Trial of multifactorial prevention of coronary heart disease. Final report on the 6 years results. *Lancet* 1989; 2: 869-72.
- The Lipid Research Clinics Coronary Primary Prevention Trial. Results I: reduction in incidence of coronary heart disease. *JAMA* 1984; 251: 351-64.
- The Lipid Research Clinics Coronary Primary Prevention Trial. Results II: the relationship of reduction in incidence of coronary heart disease to cholesterol lowering. *JAMA* 1984; 251: 365-74.
- Frick MH, Ello O, Haapa K, et al. Helsinki Heart Study: primary prevention trial with Gemfibrozil in middle-aged men with dyslipidemia. *N Engl J Med* 1987; 317: 1237-45.
- Shepherd J. For the West of Scotland Coronary Prevention Study Group. The West of Scotland Coronary Prevention Study. A trial of cholesterol reduction in Scottish men. *Am J Cardiol* 1995; 76: 113C-7C.
- Kannel WB, McGee DL, Castelli WP, et al. Latest perspective on cigarette smoking and cardiovascular disease: the Framingham Study. *J Cardiac Rehabil* 1984; 4: 267-77.
- Wilhelmsen L, Berglund G, Elmfeldt D, et al. The multifactor primary prevention trial in Goteborg, Sweden. *Eur Heart J* 1986; 7: 279-88.
- Doll R, Peto R, Wheatley K, et al. Mortality in relation to smoke: 40 years observations on male British Doctors. *BMJ* 1994; 309: 901-11.
- Wilhelmsson C, Vedin JA, Elmfeldt D, et al. Smoking and myocardial infarction. *Lancet* 1975; 1: 415-20.
- Aberg A, Bergstrand R, Johansson S, et al. Cessation of smoking after myocardial infarction. Effects on mortality after 10 years. *Br Heart J* 1983; 49: 416-22.
- Mulcahy R, Hickey N, Graham I, et al. Factors influencing long-term prognosis in male patients surviving a first coronary attack. *Br Heart J* 1975; 37: 158-65.
- Salonen JT. Stopping smoking and long-term mortality after acute myocardial infarction. *Br Heart J* 1980; 43: 463-9.
- Hermanson B, Omenn G, Kronmal R, et al. Beneficial six-year outcome of smoking cessation in older men and women with coronary artery disease. *N Engl J Med* 1988; 319: 1365-9.
- Vartiainen E, Puska P, Jousilahti P, et al. Twenty-year trends in coronary risk factors in North Karelia and in other areas of Finland. *Int J Epidemiol* 1994; 23: 495-504.
- Wilhelmsen L, Johansson S, Olvenstam G, et al. CHD in Sweden: mortality incidence and risk factors over 20 years in Gothenburg. *Int J Epidemiol* 1989; 18(suppl 1): S101-S8.
- Ueshima HP, Tataru K, Asakura S. Declining mortality from ischemic heart disease and changes in coronary risk factors in Japan, 1956-1980. *Am J Epidemiol* 1987; 125: 62-72.
- D'Agostino RB, Kannel WB, Belanger AJ, et al. Trends in CHD and risk factors at age 55-64 in the Framingham Study. *Int J Epidemiol* 1989; 18(suppl 1): S67-S72.
- Sytrowski PA, Kannel WB, D'Agostino RB. Changes in risk factors and the decline in mortality from cardiovascular disease. The Framingham Heart Study. *N Engl J Med* 1990; 322: 1635-41.
- Kannel WB, LeBaver EJ, Dawmber TR, et al. Relation of body weight to development of coronary heart disease: Framingham Study. *Circulation* 1967; 35: 734-44.
- Hubert HB, Feinleib M, Mcnamara P, et al. Obesity as an independent risk factor for cardiovascular disease: a 26-year follow-up of participants in the Framingham Heart Study. *Circulation* 1983; 67: 968-77.
- Pekka J, Tuomilehto J, Vartiainen E, et al. Body weight, cardiovascular risk factors and coronary mortality: 15 years follow-up of middle-aged men and women in Eastern Finland. *Circulation* 1996; 93: 1372-9.
- Lotufo PA. Increasing obesity in Brazil: predicting a new peak of cardiovascular mortality. *São Paulo Med J* 2000; 118: 161-2.
- Joffres MR, Hamet P, MacLean DR, L'italien GJ, Fodor G. Distribution of blood pressure and hypertension in Canada and the United States. *Am J Hypertens* 2001; 14: 1099-105.
- Lolio CA, Laurenti R. Evolução da mortalidade por doença isquêmica do coração

- no município de São Paulo. Evolução de 1950 a 1981 e mudanças recentes na tendência. *Arq Bras Cardiol* 1986; 46: 153-6.
47. Lotufo PA. As doenças cardiovasculares no Brasil: estudo de caso da tendência da mortalidade no Estado de São Paulo 1970-1989. São Paulo: Faculdade de Saúde Pública. USP; 1993. Dissertação (Mestrado em Medicina Preventiva) - Faculdade de Saúde Pública. Universidade de São Paulo, 1993.
 48. Lotufo PA, Lolio CA. Tendência da mortalidade por doença cerebrovascular no Estado de São Paulo: 1970 a 1989. *Arq Bras Cardiol* 1993; 51: 441-6.
 49. Lolio CA, Laurenti R, Buchala CM, Santo AH, Jorge MH. Mortality of women in reproductive age in the municipality of São Paulo (Brazil), 1986. III. Death by different causes: cardiovascular diseases. *Rev Saude Publica* 1991; 25: 37-40.
 50. Lolio CA, Lotufo PA, Lira AC, Zanetta DM, Massad E. Mortality trends due to myocardial ischemia in capital cities of the metropolitan areas of Brazil. *Arq Bras Cardiol* 1995; 64: 213-6.
 51. Keys A. Coronary heart disease in seven countries. *Circulation* 1970; 41(suppl I): 1-211.