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Cardiovascular Risk and Intervention Study In Croatia - family medicine

Submission date	Recruitment status	[_] Prospectively registered
16/02/2009	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
31/03/2009	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
18/06/2014	Circulatory System	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
3661

Study information

Scientific Title

A multicentre prospective randomised cohort-controlled interventional study to investigate the detection of risk factors of cardiovascular disease by family medicine practitioners

Acronym
CRISIC-fm

Study objectives
Epidemiological arm:
To investigate:
1. The regional distribution of overall risk of 10 year fatal cardiovascular diseases (CVDs) among Family Medicine Practitioner (FMP) populations aged greater than or equal to 40 years
2. If there is a significant difference in CV risk factors distributions between costal/continental populations and rural/urban populations
3. The regional metabolic syndrome (MS) distribution among populations aged greater than or equal to 40 years and co-morbidities associated with it
4. If there is significant difference in nutritional status between coastal FMP populations aged greater than or equal to 40 years and its continental counterpart, as well as rural and urban populations, and its conection with socio-economic status
5. The existence of significant difference in total, high density lipoprotein (HDL) and low density lipoprotein (LDL)-cholesterol, triglycerides and creatinine concentrations between costal /continental and urban/rural populations
6. The relationship between estimated glomerular filtration (eGF) and CVDs based on serum creatinine concentrations data and the calculation of eGF using the shortened Modification of Diet in Renal Disease (MDRD) equation and the Cockcroft-Gault's formula
7. The differences in anthropometric body shape indices, as well as those in dietary regimen, alcohol intake, exercising pattern, between coastal/continental populations and urban/ rural populations
8. The association of "Mediterranean diet" to overall 10-year risk of fatal CVD, MS and nutritional status of the FMP population
9. If physicians attending continuous medical education courses achieve better results and develop more positive attitudes towards the implementation of preventive activities

Interventional arm:
To investigate:
1. If FMP can detect more CVD high risk persons using SCORE risk-chart, more persons at greater risk of developing stroke using the Framingham Table, and identify persons aged greater than or equal to 65 years who are at risk of developing/already developed malnutrition using Mini Nutritional Assessment (MNA) Scale
2. If the FMP education (using balanced educational approach and the manual prepared particularly for that purpose, as well as by adopting the guidelines proposed by expert societies for CVD prevention), will lead to better efficiency in overall CVD risk reduction, better nutritional status correction, and changes in attitudes towards prevention
3. If identified CV high risk part of the cohort (SCORE greater than or equal to 5%), part of cohort with higher risk of developing stroke (the Framingham Table), as well as those undernourished aged greater than or equal to 65 years (the MNA Scale), will be diminished as early as in 18 months
4. If the greatest advancement will be achived in total serum cholesterol reduction, somewhat less in target blood pressure levels and exercising improvements
5. If the incidence and prevalence of CVD patients in the observed cohort will be reduced in a five-year period, with a possible impact on the entire population aged greater than or equal to 40 years

6. If the incidence of newly developed CV events will be statistically lowered in the interventional compared to the control group
7. If the systematic approach to preventive activities yield more positive patients' attitudes, leads to more successful final outcome (lifestyle: dietary habits, exercising and smoking), as well as the overall cooperativeness of patients targeted by non-pharmacological and pharmacological methods

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethical Committee at University of Zagreb School of Medicine gave approval on the 19th September 2008).

Study design
Multicentre prospective randomised cohort-controlled interventional study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
GP practice

Study type(s)
Screening

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Cardiovascular disease

Interventions
The investigation outlined herein represents a multicentric, prospective, interventional, randomised cohort study, with an anticipated duration of five years. To serve its purposes, a two-staged, non-proportional, mixed population sample shall be chosen. During the course of the first study stage, a quadruple-stratified, non-proportional random sample of Family Medicine offices shall be selected, based on:
1. 21 Croatian prefectures
2. Two regions: coastal and continental
3. Five strata based on the settlement size, as follows:
3.1. Those hosting up to 3,999 inhabitants
3.2. Those hosting 4,000 to 9,999 inhabitants
3.3. Those hosting 10,000 to 29,999 inhabitants
3.4. Those hosting 30,000 to 89,999 inhabitants
3.5. Those hosting 90,000 inhabitants, and more
4. Three strata based on the number of insured persons pursuant to 2007 contract made with

the Croatian Institute for Health Insurance (the CIHI), as follows:
4.1. Up to 1,399 insured persons
4.2. 1,400 to 1,799 insured persons
4.3. 1,800 insured persons, and more

Within each stratum, a random FMP office sample shall be selected, using a random numbers generator powered by 2007 CIHI list. The entire baseline FMP office sample (N = 64) shall be randomised into similarly large, but yet distinct groups, using a consistent, systematic selection method (the first physician thereby being assigned to the test group, the second one to the control group, the third one to the test group..., and so forth). The first group, subjected to conventional intervention (the control group) (N = 32), and the second group, subjected to an intensified intervention (the test group) (N = 32), shall be equal in terms of number of examinees entrusted with each FMP (N = 55). Taking into account the possible irresponsiveness of the FMPs invited to join the study (presumed as approximately 35% of all approached), the selection of each and every member of the main physician sample shall be accompanied by the selection of two members of the 'spare' sample. They shall be selected based on the distance of the respective FMP enrolled into the main sample, provided that they belong to the same quadruplet stratum, and shall be listed in alphabetic order. In case of a need, they shall be enrolled into the study as 'switches'.

The investigated population:
During the course of the second study stage, the selection of a systematic, non-proportional sample of 55 patients aged greater than or equal to 40 years, being the first to visit FMP's office upon the study commencement, shall be left at the discretion of a participating physician. The conveyance of detailed information on the study, as well as the consent to participate in the latter, shall be corroborated by subjects' signatures (informed consent). The size of the sample embraced by each and every stratum shall not be proportional to the entire stratum magnitude (for instance, coastal villages host 167 [7%], while continental towns and cities host 1,260 out of 2,483 [51%] FMP offices established in the Republic of Croatia [RC]), but rather equal and large enough to allow for the hypothesis testing (statistical power of at least 80%, confidence level of 95%). Prior to statistical evaluation, the disproportion in number of involved examinees per FMP shall be corrected using post-hoc weighting factors.

Survey questionnaires:
Standardised questionnaires, developed to serve the needs of this investigation and pre-validated within the frame of a pilot study involving a smaller study sample (10 FMPs, 10 survey questionnaires per each), shall be put in use. The interview technique shall provide data on socio-demographic, socio-economic, personal and family background, dietary and lifestyle habits, and drug therapy, and allow for the insight into psychological and environmental aspects relevant for the respective subject. In order to assess the nourishment status of examinees over 65 years, the standardised Mini Nutrition Assessment (MNA) Questionnaire shall be employed, constituted of two segments. The first one is termed the MNA-SF, and represents a standardised 6-item questionnaire which allows for a quick screening of the nourishment status. The examinees that succeed in achieving the score of 12 or 12+, shall be dismissed from the obligation to complete the second part of the interview, a.k.a. the Full-MNA Questionnaire. Those who manage to score less than or equal to 11 points shall be further interviewed and expected to answer 10 additional questions and undergo two anthropometric measurements (upper arm and calf diameter), also included into the Full-MNA. In order to analyse FMPs' and examinees' attitudes towards the implementation of preventive activities, the questionnaire detailed above was supplemented by the EUROPREVIEW Questionnaire.

Electrocardiogram (ECG):
Each and every examinee shall be subjected to an ECG, with the particular attention paid to the possible existence of atrial fibrillation (AF) and left ventricular hypertrophy (LVH), both well-recognised as CVD risk factors.

Laboratory analyses:
A 20-ml blood sample shall be taken from each examinee and sent over to a licensed medical-biochemical laboratory accredited by the Ministry of Health and Social Welfare for further biochemical analysis (within the frame of the laboratory workup, total, high density lipoprotein [HDL] and low density lipoprotein [LDL]-cholesterol concentrations, triglyceride, as well as blood glucose [BG] and urate levels shall be established, together with the whole blood count [WBC]). Blood samples of the examinees aged greater than or equal to 65 years who manage to attain the MNA score of 17 - 23.5, shall be a subject of additional analyses aimed at albumin levels, median cell volume (MCV), haemoglobin levels (Hgb), iron levels (Fe), and unsaturated iron binding capacity (UIBC) determination, all of those being viewed as under-nourishment indicators.

Anthropometry:
Each and every examinee shall undergo two separate measurements of body height, body weight (mass), waist and hip circumference, arterial pressure and heart rate (using identical anthropometric scales equipped with a body height meter, plasticised non-stretchable centimetre strips and mercury sphygmomanometer).

Course of the investigation, intervention and its follow-up:
Each and every person identified as undernourished, overweight or obese, as well as those at greater overall CV risk, shall constitute the cohort planned to be subjected either to conventional or intensified intervention, hosted on the premises of a FMP office. The term 'conventional intervention' implies the intervention common for the FM practice, undertaken at random, non-uniform pace by the FMPs having CV risky or nutritionally deranged persons under their wing. All participating FMPs shall attend workshops in service of study goals, organised on two separate locations. During the course of such a workshop, the FMPs constituting the interventional group shall receive education not only in terms of general instructions regarding survey conduction and calculation of overall 10-year risk of fatal CVD outcome (SCORE) and cerebro-vascular conditions (CVCs), stroke included (the Framingham Table), but also in non-pharmacological and/or pharmacological interventional strategies appropriate for the given overall CV risk identified within the study frame. They shall also be taught about other CV risk factors (smoking, lack of exercise, overweight and obesity, under-nourishment, hyperlipidaemia and arterial hypertension). The education in reference shall be underpinned by the newest guidelines of expert societies, issued in 2007: those of European Society of Hypertension (ESH) and European Society of Cardiology (ECS), Croatian Society of Cardiology, the European branch of the World Organization of National Colleges, Academies and Academic Associations of General Practitioners/Family Physicians or World Organization of Family Doctors (WONCA) as well as nutritional guidelines to be followed with gerontology population.

The workshops in reference shall be repeated every 6 months; in addition, the attendants shall be provided with the specific Manual in service of the workshop goals, prepared based on the guidelines detailed above and elucidating precise and uniform advisory and therapeutic procedures, as well as parameters and time-frames of the regular patient follow-up. Each and every subject assigned to the interventional arm shall proceed according to an individually-tailored plan, to the end of achieving strict pre-set goals in terms of nourishment status and CV factors' correction, reasonably attainable within the predestined time-frame. Each and every examinee shall be prospectively followed up in three-month intervals, and shall be retested at

months 6, 12, and 18 starting from the date of the initial visit, in the manner identical to the original one, so as to determine the intervention outcome.

The FMPs assigned to the control group shall also form a cohort, fulfil the survey questionnaire, and estimate the overall 10-year risk of fatal CVD outcome (SCORE) and CVCs development (the Framingham Table), present among the subjects under their wing, as well as the nourishment status of those among them aged 65 years and older. Following the completion of the aforementioned, they shall switch over to their usual pace and proceed in their standard, conventional manner (common, occasional and non-uniform treatment of persons burdened with cardiovascular risk factors and nourishment disorders), and shall not be provided with the Interventional Manual, as opposed to the interventional FMP group. Following the expiration of the 18-month period, they shall be bound by the obligation to provide retrospective data on their activities in the respective period.

Statistical analysis:
The significance of the differences between total, HDL- and LDL-cholesterol, as well as of those between triglyceride concentrations encountered among continental versus coastal Croatian population (inter-regional differences), together with those established between rural and urban populations of the respective regions (intra-regional differences), shall be evaluated by virtue of a non-parametric version of the variance analysis (ANOVA), in the following 4 subject groups:
1. Continental urban population
2. Continental rural population
3. Coastal urban population
4. Coastal rural population

The presence of malnutrition in the population aged 65 years and older, shall be ascertained using the MNA Questionnaire, while the differences in MNA scores, obtained both on intra- and inter-regional level, shall be tested using an uni-variant, multi-factorial variance analysis. The link between the differences in concentrations of the laboratory parameters under consideration, pre-distinguished as either normal or abnormal pursuant to the pertinent guidelines and conformant to the dietary regimen and exercise schedule, shall be established by virtue of binary logistic regression. Uni-variant multi-factorial variance analysis of the repeated measurements shall be put in use to the goal of establishing relevant differences in body mass index (BMI), MNA score, serum lipid concentrations, and arterial blood pressure prior and following the intervention. All of the obtained values shall be interpreted based on the 95%-significance level, serving as the rationale (confidence interval [CI] 95%; $P < 0.05$). The purposes of data processing shall be served by the SAS software (licensed by the Ministry of Science, Education & Sports of the Republic of Croatia).

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure
Reduction in:
1. Total CV risk (SCORE, Framingham Stroke Chart)
2. Mini Nutritional Assessment Scale (aged 65 years and more)
3. Total cholesterol, HDL, LDL, blood glucose, tryglicerides according to current guidelines in PP

and SP, dietary and drinking habits, smoking, physical activity, normal body mass index (BMI), waist circumference (WC), waist to hip ratio (WHR), blood pressure (BP)

Secondary outcome measures
1. GF correction (MDRD)
2. Attitudes towards prevention
3. Quality of Life (QOL)

Overall study start date
01/05/2008

Completion date
01/12/2009

Eligibility

Key inclusion criteria
1. All participants aged 40 and over, either sex
2. Signed informed consent

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
3520

Key exclusion criteria
1. Uncontactability (dysphasia, aphasia)
2. Severe dementia
3. Severe psychological disease
4. Expected survival 6 months or less

Date of first enrolment
01/05/2008

Date of final enrolment
01/12/2009

Locations

Countries of recruitment
Croatia

Study participating centre
Albaharijeva 4
Zagreb
Croatia
10000

Sponsor information

Organisation
Association of Teachers in General Practice (Croatia)

Sponsor details
Rockefellerova 4
Zagreb
Croatia
10000

Sponsor type
Research organisation

Funder(s)

Funder type
Government

Funder Name
Applications for funding submitted to (not confirmed yet):

Funder Name
Association of Teachers in General Practice (Croatia)

Funder Name
Ministry of Science, Education and Sport (Croatia)

Funder Name
European GP's Research Network (EGPRN)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/02/2012		Yes	No
Results article	results	04/12/2012		Yes	No
Results article	results	12/07/2013		Yes	No
Results article	results	01/01/2014		Yes	No