CLINICAL AND EPIDEMIOLOGICAL CONSIDERATIONS ON HERPES SIMPLEX GENITAL INFECTIONS

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REZUMAT

Herpesul genital, o infecţie sexuală tratabilă, dar incurabilă, cauzată mai frecvent de tipul 2 de virus herpetic (HSV2), este o problemă majoră de sănătate, afectând un procent mare din populaţia activă. Obiectivele studiului au fost cunoaşterea datelor de seroprevalenţă specifică faţă de virusul herpes simplex tip 2 la femei active sexual care se prezintă la ambulatoriul de specialitate, identificarea comportamentelor la risc, stadializarea Papanicolau, cu scopul aplicării unor intervenţii adecvate de control şi prevenţie atât la nivel individual cât şi populaţional. A fost investigat un lot de 224 femei, iar metodele utilizate au fost ELISA pentru serologia IgG şi IgM şi testul Papanicolau, fiecare femeie completând şi un scurt chestionar. Seroprevalenţa IgG HSV 2 a fost de 51,8%, iar IgM HSV de 6,26%. Un procent mare din cazuri nu au putut descrie un episod acut în antecedente(93,4%), iar dintre cazurile cu IgM pozitiv doar 14,3% au prezentat simptomatologie caracteristică infecţiei herpetice. Testul Papanicolau a evidenţiat clasa II în 78,6% din cazuri, dovedindu-se o relaţie cauzală semnificativă ststistic între acest stadiu şi prezenţa anticorpilor IgG (OR= 3,35, 1,60< OR< 7,09; RR= 1,99, 1,26< RR< 3,14; p=0,0004). Dintre factorii de risc au fost evidenţiaţi numărul de parteneri(OR = 2,12 , 1,17< OR< 3,85; RR= 1,41, 1,10< RR< 1,80; p=0,008) şi utilizarea redusă a mijloacelor de protecţie (doar 30,36% utilizează constant prezervativul). In concluzie, rezultatele studiului arată că este necesară o monitorizare constantă a morbidităţii, a factorilor de risc şi eficienţei tratamentului, în vederea unor intervenţii adecvate atât la nivel individual, cât şi populaţional.

***Cuvinte cheie**: herpes genital, test Papanicolau, factori de risc*

ABSTRACT

Genital herpes, a treatable but, at present, incurable sexually transmitted infection usually caused by herpes simplex virus type 2 (HSV2), is a major public health threat, affecting a high percentage of the sexually active population. The objectives of the study were the detection of the seroprevalence of antibodies to HSV-2 as one way to estimate the prevalence of genital herpes in a population, high risk behaviors estimation, analysis of Pap test result, for a better control and prevention strategies implementation. We investigated 224 women, using ELISA method for serology and Pap test. All the women filled in a short questionnaire. The seroprevalence of IgG antibodies against HSV 2 was 51.8% and IgM was positive in 6.26% of cases. Risk of transmission is associated with frequency of asymptomatic viral shedding, 93.4% of women with IgG antibodies had no clinical signs in the past and

only 14.3% of IgM positives cases had an acute symptomatic genital herpes. The Pap test results showed the stage 2 in 78.6 % of patients and 88% of IgG HSV 2 positives cases (OR= 3.35 1.60< OR< 7.09; RR= 1.99, 1.26< RR< 3.14; p=0.0004). Factors associated with HSV-2 seroprevalence include age, number of sexual partners (OR = 2.12, 1.17< OR< 3.85; RR= 1.41, 1.10< RR< 1.80; p=0.008) and lack of condom use (the regular use of condom is present in only 30.36 % of cases). In conclusion, a continue surveillance in the general and specific populations, the risky behaviors evaluation, the evaluation of the effectiveness of suppressive therapy in preventing spread of infection are very important tools for designing effective interventions.

***Keywords**: genital herpes, Papanicolau test, risk factors*

Abbreviations:

STD – sexually transmitted diseases; HSV 1- herpes simplex virus type 1; HSV 2– herpes simplex virus type 2; IgG - immunoglobulin G; IgM- immunoglobulin M; OR-odds ratio.

INTRODUCTION

Sexually transmitted infections (STDs) represent an important public health problem, due to their repercussions on population, as well as on individual health. The diverse etiology, varied evolution, but also the presence or absence of therapeutic means, makes these diseases sometimes hard to control in terms of secondary and tertiary prophylaxis. On the other hand, due to the common transmission route, these diseases may be prevented, with many available prevention methods. Any prophylactic strategy must be based upon a good knowledge of morbidity data, evolution trends and factors which influence the epidemiologic process of these infections.

In this study, one of the most frequent viral sexual infections, affecting both the health of the couple and that of the newborn, has been approached.

Herpes is an infectious disease, caused by type 1 or 2 herpes simplex viruses, characterized by persistent and latent infection, with multiple reactivation episodes, and, clinically, by varied manifestations, from infections localized in different tissues and organs to generalized herpes. Genital herpes, caused by type 2 virus, is a major health problem, global data showing that at least 5% of fertile age women reported a clinical history of genital herpes infection, 30% of these women have positive serologic tests for type 2 herpes virus, and 2% of women become infected during pregnancy [1]. Every year, in the USA, estimates of 1500 – 2000 cases in newborns are recorded [2]. The frequency of congenital HSV 2 infections is considered to be of 1 case in 2000-5000 births. [3]. In most cases, the infection is transmitted during birth, when the foetus passes through the cervical channel. During the first weeks of pregnancy, infection may be associated with abortion. Infections occurring later in the course of pregnancy may cause microcephaly or hydro-anencephaly and ocular lesions (microphtalmy, kerato-conjunctivitis and retinitis). Effects have been described both in the case of primary and reactivated infections. In our country, few data exist on the prevalence of the infection in fertile age women or in the general population.

OBJECTIVES

1. Assessment of specific IgM and IgG antibodies to type 2 herpes simplex virus in sexually active women addressing obstetrics-gynecology services.
2. Clinical-epidemiologic analysis of cases with positive serology
3. Evaluation of Papanicolaou test pathological findings in women with positive serology

4. Analysis of risk behaviors in the investigated population

MATERIAL AND METHOD

A total of 224 fertile age women who addressed the obstetrics and gynecology outpatient department have been investigated. Each person filled in a short questionnaire and biological samples for serologic and Papanicolaou tests were collected.

IgG and IgM antibodies to type 2 herpes simplex virus were tested using ELISA tests with kits produced by Human. Enzyme immunoassays which detect specific serum anti-HSV 1 and 2 IgM and IgG antibodies are only useful for diagnosing primary infection. IgG antibodies persist for long periods. In cases of reactivation, the titers of specific antibodies show uncharacteristic changes (undetectable levels), for which reason they do not have a practical diagnostic value. Serologic diagnosis is useful for the screening of chronic infections. The disease is frequently detected, over 90% of the adult population having antibodies to type 1 herpetic infection and between 25-50% to type 2 herpes virus. [4].

RESULTS

The average age of the investigated group was 27.7 years (minimum 16, maximum 54 years).

Single women were predominant (Table 1).

Table 1. Marital status

Marital status	Number	Percent
Married	58	25.9
Single	138	61.6
Other	28	12.5

The most frequent age group was 20-24 years, followed by 25-34 years (Figure 1).

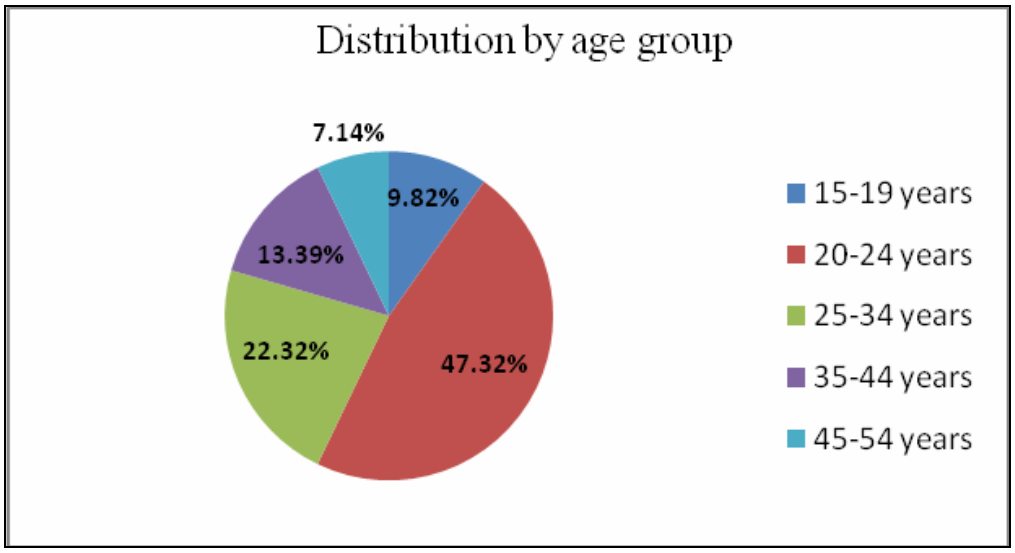

Figure 1. Age group distribution of the investigated women

The results of serological testing for IgG and IgM antibodies show a 6.26% prevalence of recent infections and 51.8% of past infections (Table 2). Of the 14 cases with positive IgM tests, only 2 had typical herpes lesions (14.3%), the rest being asymptomatic.

Of the 121 cases of past herpes virus infections, only 8 cases reported histories of one or more genital herpes eruption episodes (6.6%).

Table 2. Prevalence of IgG and IgM anti-type 2 herpes virus antibodies

	Number of positive cases	**% positive cases**
IgM HSV 2	14	6.26
IgG HSV 2	116	51.8

Detection of IgM antibodies is useful for confirmation of an active infection; it is clinically significant especially for the diagnosis of neonatal infection and herpetic encephalitis.

The analysis of the number of sexual partners during the last 2 years shows a percent of 68.3 with a single partner and 37.9 with 2 or more partners (Table 3).

Table 3. Number of sexual partners during the last 2 years

Number of partners	**Number of cases**	**% out of total**
0	6	2.7
1	133	59.4
2	67	29.9
3 or more	18	8

The comparative analysis of IgG positive cases with one, two or more sexual partners shows a statistically significant difference (OR=2.12, 1.17<OR<3.85; RR=1.41, 1.10<RR±1.80; p=0.008) (2x2 table) (Table 4).

Table 4. The comparative analysis of IgG positive cases with one, two or more sexual partners

	IgG HSV 2 +	IgG HSV 2 -
1 partner	60	73
2 or more partners	54	31

Medical histories of the investigated women reveal that a high percent do not constantly use condoms, fact which may facilitate the transmission of sexual infections.

A relatively high percent of cases had at least one abortion and around 44% of the investigated women used contraceptives (Figure 2). Smoking may be a factor influencing fertility and health in women

and children, the percent of smokers among women being high (31.25%).

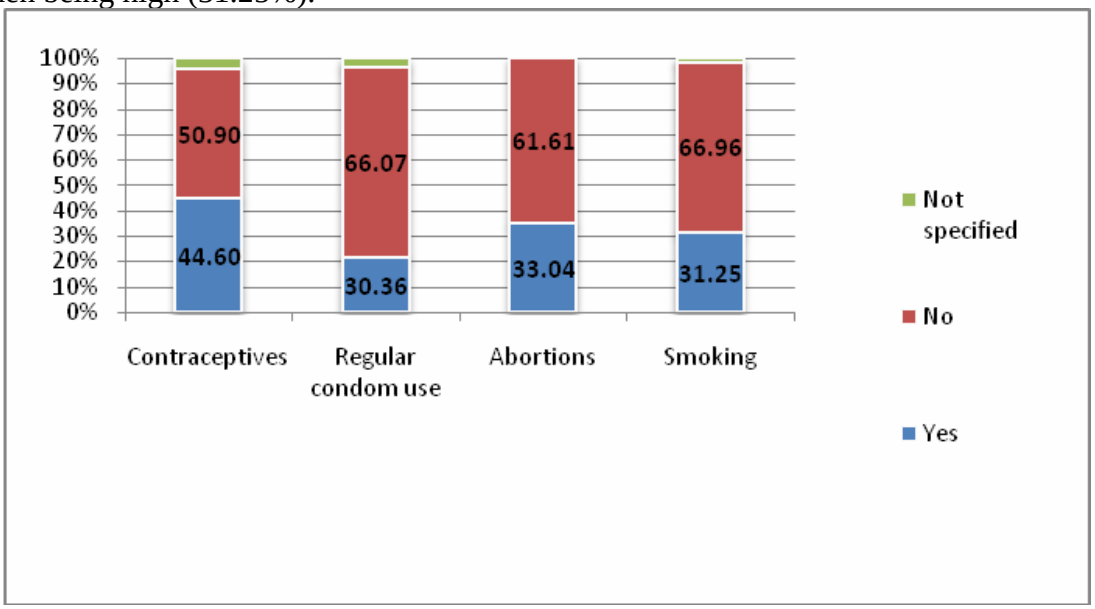

Figure 2. Proportion of risk factors recorded in medical histories of the investigated women

The analysis of Papanicolaou tests shows 78% of women with class II smears. This test is essential for the follow up of cervical cancer early lesions (Table 5).

Table 5. Cytological results of the Papanicolaou test

Stage	Number of cases	% of total
Class I	43	19.20
Class II	176	78.57
Class III	4	1.78
Class IV	1	0.45
Total	224	100

Class II smears are significantly associated with positive tests for IgG HSV 2 (OR=3.35, 1.60 < OR< 7.09; RR= 1.99, 1.26< RR< 3.14; p=0.0004) (2x2 table) (Table 6).

Table 6. Class II smears are significantly associated with positive tests for IgG HSV 2

	IgG +	IgG -
Papanicolaou Class II	102	74
Papanicolaou Class I, III, IV	14	34

Other infections detected with tests performed in women with genital symptoms are presented in Table 7.

Table 7. Number and prevalence of sexually transmitted infections in the investigated group

Type of infection	Number of cases	% of total
Trichomonas vaginalis	34	15.18
Chlamydia trachomatis	54	24.11
Candida	46	20.53
Total	134	59.82

We must state that 13.8% of the women had multiple, associated infections.

DISCUSSIONS

Screening for HSV IgG is usually performed only in pregnant women with high risk factors. Serologic tests may identify maternal exposure but they cannot discriminate between the presence of active disease and asymptomatic carrier state, nor have they predictive value on the risk of pre- or intra-partum transmission of the virus. Present recommendations indicate caesarean section only in pregnant women with active lesions at the moment of birth.
Testing for antibodies against herpes virus is widely used at transplantation centers, in bone marrow donors and receivers.

The high prevalence of type 2 HSV IgG in the studied group (51%) is explained by the fact that tests were performed in women who addressed the obstetrics-gynecology clinic with various clinical symptoms. Literature data show a rather high variation of seroprevalence figures from one country to another, with higher levels in the USA (13-40%) than in Europe (13-40%), higher values being recorded in high risk groups and also in African-Americans as compared to Caucasians [5].

Studies performed in the USA on representative population samples, showed a proportion of 22% positive cases for type 2 of the virus in persons over the age of 12. Between 80 and 90% of cases did not have clinical symptoms, the lack of awareness contributing to the silent transmission of this sexual infection. At present, herpes infection is considered to be on the first place in the USA, followed by Papilloma and Chlamydia infections [6].

From 1988 until 1994, HSV-2 prevalence in 12 year olds in the United States was 21.9% (95% confidence interval, 20.2 – 23.6%), corresponding to 45 million infected among non-institutionalized individuals. Seroprevalence is higher in women (25.6%) as compared to men (17.8%) and in African-Americans (45.9%) as compared to White individuals (17.6%). Less than 10% of all seropositives had a history of genital herpes. In a multivariate model, independent risk factors for HSV-2 seropositivity were female gender, black race or Mexican-American ethnicity, older age, low educational level, poverty, cocaine addiction and multiple sexual partners. As compared to the period 1976-1980, during the following years HSV-2 seroprevalence increased by 30% (95% confidence interval, 15.8-45.8%) [5]. Annually, around 500.000-700.000 new cases are recorded, and the

total number of infected individuals is estimated at 50 millions [7].

Risk analysis shows a statistically significant relation between IgG and the number of sexual partners. Literature data show that the strongest predictor for infection is the number of lifetime sexual partners [8]. The inconstant use of condoms, even during sexual relations inside a couple, increases the risk of HSV infections. Women have a 4 times higher infection risk than men, even at an identical exposure level [9].

The absence of symptomatology contributes to the silent transmission of the virus. The results of this study show that only 6.6% of persons with histories of infection are able to describe an acute eruptive episode. Many times, the disease is not recognized, being confounded with other sexually transmitted infections (Candida, Chlamydia, etc.). Infected persons have an average of 4 recurrences a year after the first episode, but there are variations. Type 2 herpes simplex virus causes 6 times more relapses than the type 1 of the virus.

In parallel with microbiological investigations, the Papanicolaou test is important, as the causal relation between certain viral infections and genital cancer has been documented. Class II Pap smears were significantly associated with the presence of type 2 HSV IgG.

The surveillance of antiviral therapy efficiency represents one of the present concerns in the field. According to recent data, Acyclovir does not decrease HSV-1 transmission in sexually active women and men with genital herpes. [10].

CONCLUSIONS

1. Seroprevalence of type 2 HSV IgG in the studied population was 51.8%, higher than in the general population, due to group characteristics (presence of symptomatology, age, etc.).
2. Seroprevalence of type 2 HSV IgM was 6.26%, acute infection symptomatology being present in only 14% of cases.
3. The absence of symptomatology in most cases leads to the silent transmission of the virus, an increased incidence being observed in many countries during recent years.
4. Identified risk factors for the infection were the number of sexual partners, age, inconstant use of protective means.
5. Due to long term consequences, the constant monitoring of morbidity, risk factors and treatment efficiency is important.
6. Surveillance priorities are studies performed on population groups with high transmission risk, evaluation of neonatal transmission, determination of initial episode and relapses rates, evaluation of treatment efficiency in the prevention of transmission and recurrences.

REFERENCES

1. Mandell G.L., Benett L.E., Dolin J., 2000, Principles and practice of infectious diseases, 5th ed, 1564-1575
2. Corey L, Wald A., 1999, Genital herpes. Sexually Transmitted Diseases,; 3rd ed. NY, 285-312
3. Wald A. et al., 1995, N Engl J Med., 333: 705-713
4. Cates W Jr., 1999, Sex Transm Dis., 26 (suppl 4): S2-S7
5. Nahmias A.J., & Roizman B., Infection with herpes-simplex viruses 1 and 2. New England Journal of Medicine, 289, 667-674, 719-725, 781-789
6. Fleming D.T. et al., 1997, Herpes simplex virus type 2 in the United States 1976 to 1994. N Engl J Med., 337: 1105-1111

7. Xu F., Schillinger J.A., Sternberg M.R., Johnson R.E., Lee F.K., Nahmias A.J., et al., 2002, Seroprevalence and coinfection with herpes simplex virus type 1 and type 2 in the United States, 1988-1994. J Infect Dis, 185:1019-24
8. Corey L., Handsfield HH., 2000, Genital herpes and public health: addressing a global problem. JAMA, 283:791-4
9. Bryson Y., Dillon M., Bernstein, D.I., Radolf J., Zakowski P., & Garratty E., 1993, Risk of acquisition of genital herpes simplex virus type 2 in sex partners of persons with genital herpes: A prospective couple study. Journal of Infectious Diseases, 167, 942-946.
10. Celum C., Wald A., 2008, The HPTN 039 Protocol Team, Lancet, 371: 2109-19

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HERGHELIA LIFESTYLE STUDY – AN OPEN LABEL RANDOMIZED CLINICAL TRIAL. CHALLANGES RELATED TO THE DESIGN OF LIFESTYLE CHANGE INTERVENTIONS

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REZUMAT

Scopul studiului Herghelia Lifestyle Study (HLS) a constat în evaluarea eficienţei programului de schimbare a stilului de viaţă de la Centrul Lifestyle Herghelia, Mureş. Participanţii au fost recrutaţi şi randomizaţi din 3 întreprinderi din Tg. Mureş. Grupul Tratament a participat la programul de 11 zile promovat de Centrul Lifestyle Herghelia (CLH), iar Grupul Martor a primit îngrijiri medicale obişnuite. Datele clinice şi demografice au fost culese: la start, la 10 zile, 45 zile, 6 luni şi la 1 an. Articolul de faţă discută amănuntele procesului de selecţie şi randomizare într-un trial nou ca domeniu (programe rezidenţiale de prevenţie şi lifestyle) cât şi problemele ridicate de faptul că tipul studiului (open label) cu tratamentul administrat deschis a crescut şansa unei posibile "contaminări" între cele două grupe cât şi şansa unei devieri spre ipoteza nulă. Experienţa şi observaţiile noastre pot ajuta în viitor la designul mai adecvat al studiilor similare.

***Cuvinte cheie**: schimbarea stilului de viaţă, randomizare, eroare sistematică, design de studiu, recrutare*

ABSTRACT

The aim of Herghelia Lifestyle Study was to evaluate the effectiveness of a residential lifestyle change program at Herghelia Lifestyle Center, Mures County, Romania. The participants have been recruited and randomized from 3 businesses from Targu Mures area. The Treatment group participated in an 11 day program promoted by the Herghelia Lifestyle Center and the Control group received usual medical care. Demographic and clinical data were obtained at baseline, day 10, day 45, at 6 months and 1 year. This paper discuss the details of the selection and randomization process in a novel area (residential preventive lifestyle programs) and also the challenges raised by the fact that the open label randomized

clinical study increased the chance of contamination between the two groups and thus the chance to bias the results both toward and away from the null hypothesis. Our experience and results may help others to do a better job in designing similar studies in the future.

***Keywords**: lifestyle change, randomization, systematic error, study design, recruiting,*

INTRODUCTION

Although evidence based medical recommendations [1-7] pinpoint changes in the lifestyle and health related behavior to be a omnipresent approach to chronic diseases such as cardiovascular disease, obesity and diabetes, lifestyle intervention and modification is not considered a priority and does not have political and adequate budget support nor facilities from insurance companies in order to assure the implementation of these recommendations. Romania is no exception to this situation; with a proportional mortality from cardiovascular disease of almost 60%, with increasing prevalence of obesity and diabetes, Romania continues to be a Cinderella: the prevention programs do not meet the necessary visibility and success. Interventions aimed to reduce major risk factors (cholesterol, hypertension, sedentary behavior, smoking, diabetes, obesity) and other risk factors (homocistein, C reactive protein) involved in the pathogenesis of coronary diseases and/or diabetes proved to be efficient at a clinical level and population level by reducing the rates of morbidity and mortality [8,9].

Antibiotics were the right solution for infectious epidemics. Current epidemics (cardio-vascular disease, obesity, diabetes) require a new approach. Well performed clinical trials [10,11] are demonstrating that regardless the fact that in the medical education and the clinical medical practice (including primary medical care) the accent is stressed on the drug therapies schemes, lifestyle modification must became a constant (even if it is uncomfortable) for the medical approach of the chronic diseases of civilization. The permanent unilateral help for the patient is long overdue – a new approach is required towards the involvement of the patient in her/his own health problems (joint venture) [12]. The thoughts expressed by Abraham Lincoln, are true even when talking about the prevention of chronic diseases: “you are not really and permanently helping people when you are doing for them what they should do for themselves”.

Herghelia Lifestyle Center (HLC) was created as an answer to the above stated problems. HLC is a non-profit medical structure where we are trying to approach the chronic diseases of civilization, focusing on prevention and the promotion of a healthy lifestyle (the program was described by Dr. Gh. Nandris as being “the only program from Romania with 50 beds for prevention). In 13 years of activity impressive results were obtained by the patients in the short time (11 day) of exposure to our program. [13]. An observational study at HLC between 1997 and 2000 evaluated 500 patients which consecutively requested our services and which had at least two major factors of cardiovascular risk (one of which was the cholesterol> 200 mg/dl) with an admission period of 11 days, with biochemical and anthropometric evaluation at baseline and after 10 days. The specific medication for dyslipidemia, type II diabetes, ischemic cardiac disease and hypertension was kept at the same level or was reduced (most of the cases) – anyway, the medication was not increased during their stay with us. After 10 days the total cholesterol decreased on average with 25% (it is well known that for each mg/dl of cholesterol lowering the risk of myocardial infarction is reduced by 2-3%) [14,15]. Even for those who had a total cholesterol value between 180- 200 mg/dl, the total cholesterol decreased on average with 20%. HDL cholesterol increased on average 17%. LDL cholesterol decreased on

average 29% and the triglycerides decreased 26%.

In order to assure the efficacy of the lifestyle change program at HLC, to assure the internal and external validation we performed a pilot randomized clinical trial between January 2006 and January 2007. In this study we tried to sort out potential problems which may be generated by self selection and hand-picking bias (systematic errors). The question was: can it be that the outstanding results obtained in our Lifestyle program might be due to the influence of the two systematic errors mentioned above, and another question related was, if the intervention in general population which does not apply to lifestyle change programs from different reasons, would have the same results as those observed in patients which came voluntary to Herghelia.

OBJECTIVES AND PURPOSE OF STUDY

The purpose of this study is to analyze the effects of the health program promoted at HLC on important indicators of health status, including, but not limiting at effort capacity, body weight, smoking, arterial hypertension, blood glucose, cholesterol and triglycerides, reactive protein C, etc. Specifically, the study was aimed to underline the changes in different measures of health status and the risk evolution in patients enrolled in the Herghelia program when compared with the evolution of the same factors in patients that are following usual medical care.

Our hypothesis was that the Herghelia program has the same influence in general population as in the patients who voluntarily solicited our services and that the outstanding anthropometric and biochemical outcomes are not caused by the biases mentioned (self-selection and hand-picking) but are determined by the program itself. The null hypothesis was that after the intervention there will be no statistically significant differences regarding the studied parameters and the results obtained prior on the patients that solicited the services of Herghelia could be caused by systematic errors.

MATERIALS AND METHODS

The selection of participants

The population group in which the randomization was performed consisted of the working force of 3 factories from Targu Mures area. To each employee, a questionnaire was given at the workplace (inclusion criteria was the condition to be employed at the factory) (Annex 1 and 2).

Annex 1. Initial questionnaire for cardiovascular risk evaluation, page 1

Dear employee,

Herghelia Lifestyle Center, from Herghelia, Ceuaşu de Câmpie commune, Mureş County, România is recruiting volunteers for a research study aimed to measure the effects on health of the lifestyle change program promoted by this institution.
If you are interested to be a part of this research project, please complete the following questionnaire as satisfactory as possible. Please keep in mind the following aspects:

1. The entire information solicited by the form will be confidential. No personal information will be made public. No personal information will be given to the employer. The general, statistical information will be published in a scientific journal.

2. Your participation in the study is not guaranteed after the completion of the form. The information obtained will help the physicians to make adequate selection of study participants.

3. If you will be accepted for participation, all important details of study will be revealed to you in terms of what can you expect from the study as a participant. You can refuse to participate in the study at any moment without any consequences.

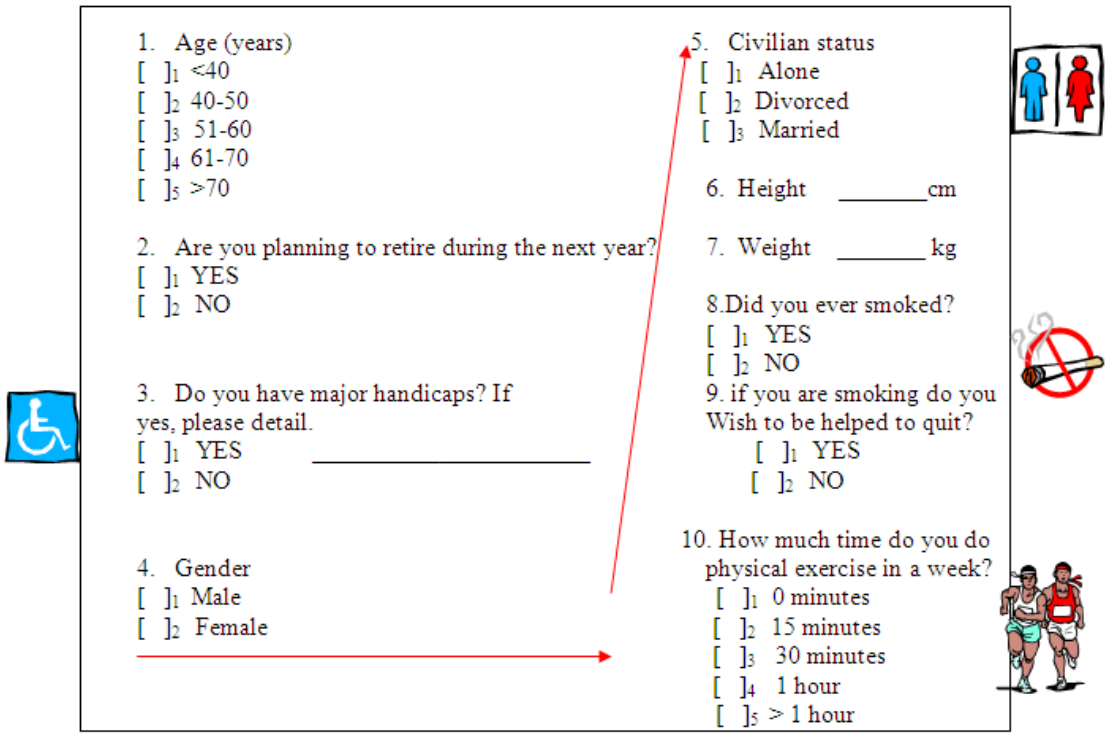
4. Shortly after the form will be completed you will be contacted and asked if you want to volunteer in this study, or, you will be told that, for the moment, you do not accomplish the necessary conditions to participate.

For details regarding the project fell free to contact Dr. Nicolae Dan, Herghelia. Telephone 0265-324010

Once again: all information provided by yourself will be kept strictly confidential

Name_____
Employ number (code) _____

Annex 2. Herghelia Evaluation Form: Health and Lifestyle, Initial questionnaire page 2



11. Were you diagnosed by a physician with the following diseases? If yes, please write For how long did you have that condition:

		<1 year	1-5 years	5-10 years
A.	Cancer	[ ]1	[ ]2	[ ]3
B.	Instable Angina	[ ]1	[ ]2	[ ]3
C.	Systemic cardiac disease	[ ]1	[ ]2	[ ]3
D.	Diabetes	[ ]1	[ ]2	[ ]3
E.	Hypertension	[ ]1	[ ]2	[ ]3
F.	High cholesterol	[ ]1	[ ]2	[ ]3
G.	Major Depressive Disorder	[ ]1	[ ]2	[ ]3

12. Were your mother or father affected by one of the following diseases? Mark the suiting variants:

	Tata	Mama
Cancer	[ ]a	[ ]g
Instabile Angina	[ ]b	[ ]h
Systemic cardiac disease	[ ]c	[ ]i
Diabetes	[ ]d	[ ]j
Hypertension	[ ]e	[ ]k
Depressive disorder	[ ]f	[ ]l

The study exclusion criteria were: severe physical handicaps (palsies, amputations, etc), those who are planning to retire during the following year, those diagnosed with cancer or instable angina. The questionnaire allowed the gathering of information regarding physical activity, body mass index, high cholesterol value, diabetes or high blood pressure or other diseases known by the patient from personal medical history or family medical history.

Each risk factor received a score from the questionnaire and the subjects were classified after the obtained score. All subjects had signed the Informed Consent Form and were classified in the decreasing order of risk score. The randomization was performed by a computer starting with the patients with maximum risk and heading towards the patients with minimum risk. The treatment group (Treatment group) came to Herghelia for a 11 days program at HLC and the Control Group were evaluated without changing their daily routine (Study Design scheme – Figure 1)

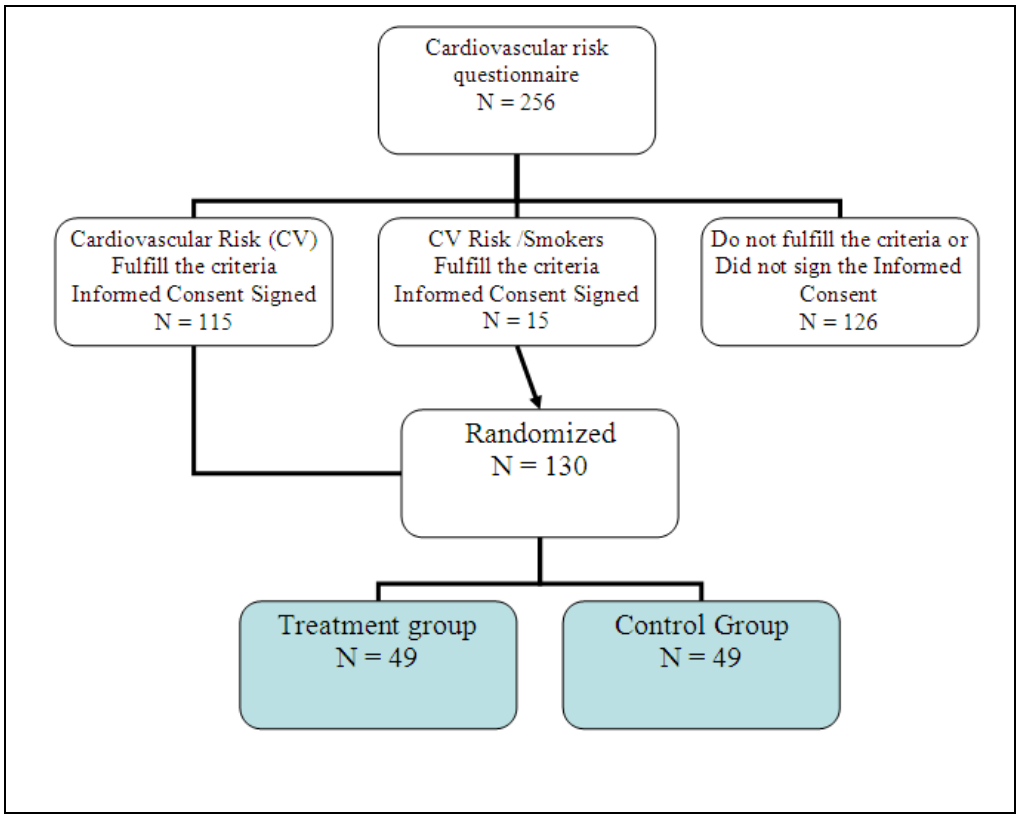


Figure 1. Study Design scheme

Technical information. The followed parameters

The study began on January 3rd 2006 continued for a year and pursued the following parameters: total blood cholesterol, HDL cholesterol and the fraction total cholesterol/ HDL cholesterol, LDL cholesterol, triglycerides, heart rate, body weight, body mass index, waist circumference, hips circumference, reactive protein C, systolic and diastolic blood pressure, blood glucose, pain.

The samplings, the clinical interviews and the anthropometric measuring were taken by the medical personnel of HLC, which were trained in standardized international methods for taking the blood pressure, body circumferences, pulse, blood sampling. Measuring and sampling were taken at the beginning, in the 10th day, at 45 days, at 6 months and after 1 year. Also, detailed questionnaires were applied regarding healthy behaviors at the beginning, after one month and a half, after 6 months and after 1 year. Biological samples (blood and urine) were analyzed at the Central Laboratory of the Targu Mures County Hospital (Automatic Analyzer Aeroset Abbott-Toshiba). The statistic calculation revealed that the most important parameters from both groups were not statistically different, so the randomization was correctly performed (Table 1). There were some statistic differences of the diastolic blood pressure of the two groups (increases in control group) and the ratio waist/hip (increased in treatment group). For the comparison of both groups we used Student's t test with p correspondent values and Mann–Whitney U test (significant threshold $p< 0.05$) working with SPSS v16 software.

Table 1. Comparative statistic data at start for the groups Treatment (Test) and Control

Demographic Variables	Control (n=49) N±SD (Range)	Treatment (n=49) N±SD (Range)	p-value for t test	p-value for MW
Age	44.5 ± 8.2 (22-57)	46.4 ± 10.3 (23-79)	0.312	0.510
Sex				
Male	21 (42.9)	19 (38.8)		
Female	28 (57.1)	30 (61.2)	0.681[a]	0.681 [a]
Baseline Clinical Values				
Weight (kg)	79.5 ± 14.9 (43-119)	79.5 ± 15.8 (56-123)	0.982	0.765
Height (cm)	166.5 ± 10.0 (141-186)	165.1± 9.5 (139 - 184)	0.458	0.572
Abdominal Circumference	93.3 ± 10.7 (72-118)	98.3 ± 14.3 (86-127)	0.054	0.145
Hip Circumference	105.6 ± 9.5 (88-127)	105.7 ± 9.5 (86-127)	0.924	0.923
Waist/Hip Ratio	0.88 ± 0.07 (0.77-1.01)	0.93 ± 0.09 (0.71-1.09)	0.008*	0.009*
Systolic Blood Pressure	105.6 ± 9.5 (88-127)	105.7 ± 9.5 (86-127)	0.211	0.056
Diastolic Blood Pressure	87.2 ± 12.1 (50-114)	81.9 ± 11.9 (60-110)	0.030*	0.014*
Blood Sugar	100.16 ± 8.46 (84-130)	105.68 ± 25.38 (76.4-216)	0.158	0.729
Cholesterol	236.26 ± 46.6 (141.9-349)	237.78 ± 49.96 (152.4-341)	0.871	0.907

Triglycerides	149.80 ± 14.80 (33.6- 114)	118.98 ± 56.33 (55-275)	0.114	0.165
HDL	58.00 ± 14.80 (33.6 – 114)	55.35 ± 13.05 (37.1 – 110.9)	0.348	0.365
LDL	148.30 ± 44.24 (3.9-239.4)	158.64 ± 37.39 (93-231.2)	0.214	0.268
Heart Rate	99.29 ± 15.44 (71-152)	94.20 ± 12.26 (68-121.6)	0.081	0.089
Pain	5.24 ± 3.16 (0-10)	5.30 ± 3.31 (0-10)	0.932	0.819

Data collection and analysis

Data was recorded on data collection forms and then double entered into a database for subsequent data summary and analysis. Demographic and between and within-group changes in clinical values and assessed health risk practices were made using standard statistical techniques.

A sample size of 50 participants in each group will provide enough statistical power (80%) to detect a 15% within-group change in mean serum cholesterol, and a 50% between-group difference in change. Additionally, 50 participants are about the maximum that Herghelia can manage in a single session.

All study related protocols (patient recruitment, risk/benefits of analysis, Informed Consent Form were revised and approved by Loma Linda University Institutional Review Board and the Ethics Committee of Medical Collegiums Cluj before the study begun. All participants entered the study after they received a detailed description of the research study and after each participant had signed the Informed Consent Form. Those who assigned to the control group received the results of blood analysis after each examination and were advised to contact the family physician or occupational physician if their values were out of range.

Intervention methods

The Herghelia Health Center and Preventive Medicine (opened for patients since 1996, with over 10.000 patients admitted so far), operates in sessions of 11 days, with fixed days for start. The patients follow a program focused on health education with strategies of modification of risk behavior involved in the genesis of atherosclerosis, coronary disease, diabetes and obesity.

Major interventions can be classified into 5 categories: diet (low-fat, high fiber, with 20-23 % of total calories from lipids, rich in vegetables, legumes, fruits, nuts, seeds and whole cereals, rich content in dietary fibers), aerobic physical exercise, physiotherapy (massage, hydrotherapy, etc.), behavior change, stress management.

The NEWSTART (c) program for lifestyle change used at Herghelia focused on the 6 major risk factors for coronary disease and much more. Half of the program at Herghelia is educational, targeting lifestyle change: anti-stress seminar, medical seminars, smoking cessation program, weight management program, hypertension management, type 2 diabetes management program, NEWSTART presentations and anti-atherogenic nutrition/cooking. Three of 6 hours of the daily "treatment" program are dedicated to healthy lifestyle education.

DISCUSSION

The design of an open label, randomized clinical trial in the field of Lifestyle Medicine is new, as the specialty (American College of Lifestyle Medicine [16] – is reuniting physicians of a new medical specialty – Lifestyle Medicine which was founded by American Medical Association in 2004). There are only a few trials in this field, especially when we consider the residential life-style change programs). The great majority of residential programs are observational, and, when randomized clinical trials were performed, they were done in ambulatory conditions. Due to the novelty of this type of residential trial it is worth to discuss some issues that this clinical trial it had raised:

1. Problems regarding open label randomization, study design and systematic errors

Standard design of randomized clinical trials was established by the drug research that allow hiding a small quantity of active component in a base of starch and glucose that makes the placebo drug to look the same as active drug. So, the patients from a randomized clinical trial can be placed in the control group or treatment group without knowing which one received the active substance. If the medical personnel know which is the group that receives the active substance we have a blinded study, but if the medical personnel do not know which group receives the active substance we have a double blind trial. It is difficult to extrapolate clinical trials about drugs to a lifestyle change intervention and we must know that there will be systematic error in both ways. This is due to the fact that one group has to change diet, physical activity, etc. in a direction that everybody knows that this will be the healthy life style. Everybody knows that the physical activity is important for health, all know that a healthy natural diet, less processed, with plenty of vegetables and fruits is healthier. Because the treatment group is trained and then behavior changes are demanded, the participants of this group know that they are the treatment group. On the other hand, the necessity that all the research ethical codes to be respected, makes the remittance of the details of the intervention imperative before the Informed Consent is signed. This knowledge can influence the performance of the test and control groups: either towards distancing from the null hypothesis or approaching to it. Even in the case of a trial that is following the specific contribution of one factor (for example: the treatment group must change diet and do physical exercises while the control group just changes the diet – the trial aiming for finding the specific contribution of physical exercise) there is a possibility that both groups to think that they are the treatment group, and each of the groups having the tendency to limit all behavior with impact on health, moving the trial results close to the null hypothesis.

On the other hand, to be able to eliminate the confounding factors it is recommended that both groups to be selected from the same population, same exposures, same living and working conditions. This is the situation for our study, in which the participants were selected amongst the employees of three factories. Each subject hoped that they will be in the treatment group for a free ride, but some of them found themselves later in the Control Group.

We were aware that, in general, the employees/workers have a better health

status than the people un-employed (healthy worker effect), but we considered that the effect of this systematic error resolve not head our results towards the working hypothesis but towards the null hypothesis. But, if in this context where there are tendencies of influencing the results towards the null hypothesis some significant differences appear between the two groups, the chances are that the positive results of intervention to be validated.

We kept in mind the fact that all participants were chosen from the same factory and a contamination between the two groups could be possible because the participants from Treatment group could communicate with the participants from the control group and give details about the intervention and behavior changes from HLC (less fat, cereals and integral bread , the calories repartition throughout the day) and so, the Treatment group could have better results on blood tests and anthropometric measures if the control group would have not received these information. The contamination could influence the results towards a null difference between the two groups. After we had performed the statistical analysis, we realized that probably we had quite a bit of contamination in our groups. In the Treatment group there were significant differences between the initial data and the data collected at 10 days, 45 days, 6 months and 1 year; although there were statistical differences between the two group at 10 days, and after 45 days at the most of the studied parameters there were no longer significant differences between the groups (the evolution curves were similar to the control group).

Because the participants had come to Herghelia as a group, it was obvious that a study was implied. There was also the possibility to bring the participants at different timing during the year. The first reason why we had chosen to bring the participants as a group was the timing. The beginning of a new year is the period of time when the employs have more free time and can participate in the study. We could have brought the participants throughout the year but this would increase considerably the time of the study and the costs. To compensate this, comparative studies were performed between the Treatment group and other groups of patients participating in the program. Per global, we considered that the tendency of results to get closer to the null hypothesis were more powerful than the tendency of results to get closer to our working hypothesis.

2. Financial Problems

One of the reasons why randomized residential clinical trials were avoided by other centers is high cost. From the Loma Linda University estimations, the cost of this clinical trial, performed in volunteering condition by Romanians and Americans was just a fraction from the costs performed in the industrialized countries. Study design had to take into account the financial limitations. Ideally, to eliminate systematic errors we should have chosen besides the 2 groups, a third one, (a second control group), selected after same criteria, from a similar factory but not from one of the three selected in this study, so the confounding effect could be minimized. Also, in order to eliminate the healthy worker effect a comparison group from general population would have been useful. All of these would have meant a more generous study fund. It is then remarkable the fact that the necessary amount of money was found in order to perform this study as mentioned.

3. Problems regarding the conflict of interest

At the moment, there are discussions regarding the impact of the conflict of interest in medical practice and in research [17]. Important journals from several universities are making requests to the physicians and researchers to mention the affiliation or the relationship to the drug industry [18]. Most of the trials are funded by the pharmaceutical industry and there is a

considerable pressure for positive results: the trials are the final step of a very complicated and expensive process by which each drug is put on the market. Positive results mean an open gate to market the product and to recuperate the investment and make profit because is no secret that this is why the industry is operating. Because the program tested in our trial is the one we offer to the patient in the last 13 years a conflict of interest may arise.

We want to demonstrate that what we are offering is worth buying and a tendency for subjectivism for the research phenomena still exists. On the other hand it is difficult to conduct experiments in other circumstances because there are few centers of this kind. Public Health, Preventive Medicine, the health education and the change of lifestyle do not have the attractivity and financial resources of other medical specialties or pharmaceutical research, so it is hard to imagine another scenario, but the one that we have had in this study: volunteering. We have tried to minimize the confounding by requesting consultancy from Loma Linda University, a university with tradition in clinical trials on lifestyle.

4. Ethical problems

It is not easy to study the apparent obvious things. Although the popular wisdom intuitively believed in the benefits of physical exercise for coronary disease, a lot of years had passed, and after smoking, high blood cholesterol and hypertension, in the 1990s the lack of physical exercise was declared a major risk factor. This behavior was intuitive related to the heart's health and had to be long studied in order to receive this status, based on evidence.

Our study proposed to measure the impact of a lifestyle most people believe is healthy but it was never measured in terms of the contribution of each element to the general outcome. We regarded our work as a pilot trial, as a departure point for other studies. We wish to better understand the specific contributions of each element from Herghelia program.

We would like specially to quantify the contribution of health education to the outstanding results. We would like to redo our study with three groups: the first Treatment group will be enrolled in the full Herghelia program, the second Treatment group will receive the Herghelia program minus the educational program (they will receive the diet from Herghelia, they will have a nutritional and a physiotherapy program but no one will explain to them the importance of the risk factors that led to the chronic diseases they are suffering, no one will explain the role of nutrition and why is being used that specific diet – a situation similar to the general set up in the regular health care system today.

Here there is an ethical issue: is it ethical to retain something for which there is no evidence based data that it has a contribution to healing or rapid reduction of cardiovascular risk factors, but all intuitively think health education and promotion is a positive element in the treatment and control of the chronic diseases. So far we do not know the specific and quantitative contribution of health education and promotion in reducing the cardiovascular risk.

As a matter of fact, a similar problem appeared in the pilot study: to ban the communication between the Treatment group and the control group, to forbid the transmittal of information regarding the health education or not. We have left this to the participants' decision, because for the most of elements offered at Herghelia there are sufficient evidences (fibers and integral bread reduces the risk of coronary disease, and reduces the cholesterol, decreases the blood glucose and the physical exercise reduces the blood glucose and the risk of coronary disease).

CONCLUSIONS

We are expecting that the results of this study to contribute to a better design of randomized clinical trials in the field of residential preventive medicine. The randomization was performed in good conditions – the comparative statistical data between the two groups did not evoked significant differences, both groups being similar at start.

Because the subjects had signed an Informed Consent where the details of the intervention were presented it was hard to cover the fact that the group which participated in the program from Herghelia was the Treatment group that generated perhaps better results than in the subjects that usually came to Herghelia. This phenomenon influenced the results by distancing from the null hypothesis.

The control group was aware that the group will not be enrolled in an intervention as the Treatment group and due to the fact that the groups were formed by employs from the same factories compensation and a contamination phenomenon could have happened influencing the results by distancing from the null hypothesis.

The study groups selected from workers have the tendency to have healthy worker effect that can move the results towards the null hypothesis (fewer changes in the parameters of the Treatment group and so smaller differences between test and control groups). Finally, to increase the possibility to be applied in general population, ideally a randomized trial have to be planned from general population with a design that allows the quantification of the specific contribution of various factors of the lifestyle intervention to the significant results obtained during an eleven day residential lifestyle program.

REFERENCES

1. Mosca L., et al., 2007, Expert Panel/Writing GroupEvidence-based guidelines for cardiovascular disease prevention in women: 2007 update. Circulation.2007, Mar. 20;115(11):1481-501. Erratum in: Circulation 2007 Apr. 17;115(15):e407.
2. ***, 2007, European Guidelines on Cardiovascular disease prevention in clinical practice: executive summary. Fourth Joint Task Force of European Society of Cardiology and other Societies on Cardiovascular Disease Prevention in Clinical Practice. European Heart Journal 2007; 28: 2375-2414
3.***, 2004, American Cancer Society, the American Diabetes Association, and the American Heart Association. Preventing Cancer, Cardiovascular Disease, and Diabetes A Common Agenda for the American

Cancer Society, the American Diabetes Association, and the American Heart Association *Circulation.* 2004;109:3244-3255.

4.***, 2007, AHA/AACVPR Scientific Statement. A Scientific Statement From the American Heart Association Exercise, Cardiac Rehabilitation, and Prevention Committee, the Council on Clinical Cardiology; the Councils on Cardiovascular Nursing, Epidemiology and Prevention, and Nutrition, Physical Activity, and Metabolism; and the American Association of Cardiovascular and Pulmonary Rehabilitation. Core Components of Cardiac Rehabilitation/Secondary Prevention Programs: 2007 Update. *Circulation.* 2007;115:2675-2682.

5.***, 2003, AHA Scientific Statement. American Heart Association Guidelines for Primary Prevention of Atherosclerotic Cardiovascular Disease Beginning in Childhood *Circulation.* 2003;107:1562.

6.***, 2006, Diet and Lifestyle Recommendations Revision 2006 A Scientific Statement From the American Heart Association Nutrition Committee *Circulation.* 2006;114:82-96.

7.***, 2006, Preventing Cardiovascular Disease and Diabetes. A Call to Action From the American Diabetes Association and the American Heart Association. Circulation. 2006;113:2943-2946. 2006 American Heart Association, Inc.

8. Salim Y. at al., 2004, Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study); Lancet 2004; 264:937-52

9.***, 2002, Diabetes Prevention Program Research Group: Reduction in the incidence of type II diabetes with lifestyle intervention or metformin. N Engl J Med 346:393-403, 2002.

10.***, 2002, Diabetes Prevention Program Research Group: Reduction in the incidence of type II diabetes with lifestyle intervention or metformin. N Engl J Med 346:393-403, 2002

11. Uusitupa M. et al:The Finnish Diabetes Prevention Study. Br J Nutr 83 (Suppl 1): S137-S142,2000

12.***, WHO Alma Ata Declaration, 1978 www.who.int/hpr/NPH/docs/declaration_almaata.pdf accesat la 3 June 2009

13. Dan N. et al. Rezultatele activităţii Centrului de Sănătate la 13 ani de activitate. Viaţă+Sănătate, 2009, vol. 9, nr 3, pag 20-22

14. Law M.R., Wald N.J., Thompson S.G. 1994, By how much and how quickly does reduction in serum cholesterol concentration lower risk ischaemic heart disease? BMJ 1994;308:367–72.

15. Njolstad I., Arnesen E., Lund-Larsen P.G., 1996, Smoking, serum lipids, blood pressure, and sex differences in myocardial infarction. A 12-year follow-up of the Finnmark Study. Circulation 1996;93:450–56.

16. ***, http://www.lifestylemedicine.org/ accesat 3 iunie 2009

17. Abbasi and Smith. Editorial, 2003, No more free lunches, BMJ, 326:1155-1156 (31 May), doi:10.1136/bmj.326.7400.1155

18. Miller J.D., 2006, Conflict-of-Interest Spurs New Rules, Not

Consensus. JNCI Journal of the National Cancer Institute 2006,98(23):1678-1679; doi:10.1093/jnci/djj508

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HERGHELIA LIFESTYLE STUDY – EFFICIENCY OF A REZIDENTIAL LIFESTYLE CHANGE PROGRAM

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REZUMAT

Herghelia Lifesyle Study a avut ca scop să testeze eficienţa programului rezidenţial de schimbare a stilului de viaţă în ce priveşte modificarea factorilor de risc în boala coronariană, eliminând erori sistematice care au parazitat până acum studiile rezidenţiale existente. Grupul Test (N=49) a participat la programul oferit la Herghelia (dietă hipolipidică, abandonarea fumatului, exerciţiul moderat, fizioterapie şi managementul stresului), iar Grupul Martor (N=49) a continuat rutina zilnică. După 10 zile au existat diferenţe semnificative statistic în ce priveşte modificarea factorilor de risc cardiovascular în favoarea lotului Test: colesterolul total, LDL, greutatea corporală, circumferinţa abdominală, IMC (p<0,001), glicemia (p<0,018), dar nu s-au constatat diferenţe semnificative în ce priveşte frecvenţa cardiacă, raportul colesterol total/HDL, tensiunea arterială sistolică şi diastolică. În concluzie, intervenţii intensive multifactoriale de genul celor de la Herghelia par a fi validate de studiul prezent şi se pare că pot avea un impact major şi la nivelul populaţiei în general prin scăderea semnificativă a factorilor de risc majori pentru boli cronice comune cum ar fi boala coronariană, diabetul şi obezitatea.

***Cuvinte cheie**: stil de viaţă, intervenţii multifactoriale, boala coronariană, colesterol, glicemie*

ABSTRACT

Herghelia Lifestyle Study aimed to test the effectiveness of a residential lifestyle change program in modifying CHD risk factors by trying to eliminate the biases existing in the residential studies done until now. The Treatment group (N=49) participated in the program we offer at Herghelia (low fat diet, stop smoking, moderate exercise, physiotherapy, stress management) and the Control group (N=49) continued with their daily routine and usual care. After 10 days there was a statistically significant decrease of most of the CHD risk factors in the Treatment group when compared with the Control group: the changes were highly significant (p<0.001) for total cholesterol, LDL cholesterol, body weight, waist circumference, BMI and glycemia (p<0.018) but we didn't find statistically significant differences for heart rate, total cholesterol/HDL ratio, systolic and diastolic blood pressure. Conclusion: this study seems to validate multi-factorial lifestyle interventions like the one offered at Herghelia Lifestyle Center and it seems that they also can have a major impact on general population through lowering significantly the major risk factors for chronic diseases like CHD, diabetes and obesity.

***Keywords**: lifestyle, multi-factorial interventions, CHD, cholesterol, glycemia.*

INTRODUCTION

Preliminary data from the Programul Naţional de Evaluare a Stării de Sănătate a Populaţiei din România (The National Program for the Evaluation of the Health Status of Romanian Population) indicate that our country is confronted with a raising in the incidence of diabetes, obesity (even in children), hypertension, cancer, coronary heart disease, dyslipidemia while consumption of tobacco and alcohol remain a Public Health challenge. For example, in Cluj only, "144.648 people have an increased risk for diabetes, 26.028 have high risk for cardiovascular diseases and over 10.000 are at risk for uterine cancer. This program evaluated 380.000 people in Cluj and the most frequent test recommended by the family physicians was glycemia".

Regarding cardiovascular diseases which are the first cause of death in Romania, the major modifiable risk factors for coronary heart disease (CHD) are almost all from the sphere of someone's lifestyle whether we are talking of increased cholesterol, lack of physical exercise, smoking or hypertension, obesity and diabetes. It is not by chance that in European Community and USA the common message of the guides for the management of the Cardiovascular Diseases (CVD) is a prevention oriented lifestyle.

In 2006 American Heart Association and American Diabetes Association issued a common Call to Action , saying: „Both the American Heart Association and the American Diabetes Association remain jointly committed to a reduction in heart disease, stroke, and new-onset diabetes. We strongly recommend that all providers assess patients for their global risk for CVD and diabetes. Despite many unresolved scientific issues, a number of cardio metabolic risk factors have been clearly shown to be closely related to diabetes and CVD: fasting/postprandial hyperglycemia, overweight/obesity, elevated systolic and diastolic blood pressure, and dyslipidemia. Although pharmacologic therapy is often indicated when overt disease is detected, in the early stages of these conditions, lifestyle modification with attention to weight loss and physical activity may well be sufficient.

It must be remembered that obesity is far more than an unattractive appearance but can be prevented. Moreover, it is often a visible marker of other underlying risk factors that can be addressed. Thus, the overweight or obese patient deserves major clinical attention. The growing prevalence of this condition threatens to undermine all of our recent gains to prevent and control chronic disease." Public Health and Primary Care play an important role in prevention, early detection and treatment of these diseases of modern civilization through health education and promotion.

At the Herghelia Lifestyle Center we are taking seriously this call to address and reduce the risk factors just mentioned by integrating our lifestyle change program with the usual Primary Care and/or clinical work. With Herghelia Lifestyle Study we tried to show that through lifestyle change there could be a fast and significant impact in lowering the common risk factors for the major chronic diseases we fight in Romania (CVD, diabetes, obesity) through lifestyle change. Also, our results suggest that the influence of these changes can extend beyond personal life to coworkers, friends and most probably impact the family of provenience.

To study the efficiency of the residential lifestyle change program at Herghelia Lifestyle Center (HLC) we have done a pilot randomized clinical study from January 2006 to January 2007.

TRIAL OBJECTIVES AND PURPOSE

The purpose of this study is to assess the results of Herghelia's live-in program on salient measures of health including but not limited to changes in weight, smoking, blood pressure, blood sugar, blood triglycerides, exercise etc. Specifically, the study seeks to compare changes in clinical health measures and health risk in participants who experience the Herghelia live-in program with comparable participants who receive standard medical care.

The working hypothesis was that the Herghelia program has same impact in the general population (general applicability) like in the subpopulation of patients who came as patients at Herghelia in the last 13 years and the remarkable results were not due to the hand picking and self-selection biases.

Secondly, we were interested in the history of lifestyle change and relapse. From this standpoint we would have liked to have more resources to make more frequent measurements to identify which is the most susceptible period in term of relapse in the treatment group. It is important to know if and when is this susceptible, critical time in the history of lifestyle change because with a minimum of resources we could support patients pointedly to continue with the healthy lifestyle.

STUDY DESIGN

The selection, randomization and description data of participants has been published in a previous article.

METHODS

The treatment group underwent a multifactorial, intensive intervention including: special formulated plant based diet, physical exercise, stop smoking program (approved by the Societatea Română de Cardiologie (the Romanian Society for Cardiology), weight management, daily stress management program, blood pressure management program, diabetes management, counseling and group therapy.

Diet and exercise

The diet and the exercise program have been the key elements of our program. The diet served at Herghelia and to the treatment group was specially formulated for the prevention and treatment of chronic diseases of civilization and contain between 1600 and 2150 calories a day, according with the person's needs. Fats provide 21-23% of total calories (saturated fats less than 5%, monounsaturated fats 5%, polyunsaturated fats 11-13%, with an average of 3.8 g of the omega 3 linolenic fatty acid daily. Carbohydrates provide 66% of the daily calories with the majority of them being complex carbohydrates from whole wheat bread, whole cereals bringing about 50 grams of fibers daily. The protein in the diet gives about 12-13% of total calories. The diet does not contain cholesterol and is rich in vitamins (Beta-carotene, B1, B3, B6, C, E and folic acid) and minerals (MG, Fe, K, Selenium) as well as a multitude of phytochemicals.

With respect to exercise the treatment group participated in about 2.5 hours of aerobic physical exercise: 30 minutes of weak up exercise in the morning, 1 hour mobility exercise and 1 hour of supervised walking with the intensity of this physical exercise from 2 to 6 METS.

The whole intervention program at Herghelia was elaborated in accordance with the WHO recommendation for the global management of the risk of CVD: "OMS recommends a global approach of the management of the CVD risk rather than isolated measures against smoking, high blood pressure etc. Without doubt smoking

is the leading risk factor, followed by the high blood pressure, cholesterol, obesity, a low intake of fruits and vegetables, and physical inactivity."

The variables measured were: Total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides, heart rate, BMI, abdominal circumference, abdominal/waist circumference ratio, Systolic blood pressure, Diastolic blood pressure, glycemia, pain. Blood samples were sent to an external laboratory for analysis. We estimated before the study that a sample size of about 50 participants in each group will provide enough statistical power (80%) to detect a 15% within-group change in mean serum cholesterol, and a 50% between-group difference in change. Additionally, 50 participants are about the maximum that Herghelia can manage in a single session.
Data have been recorded on data collection forms and then double entered into a database for subsequent data summary and analysis. Demographic and between and within-group changes in clinical values and assessed health risk practices were made using standard statistical techniques.
Statistical data were analyzed with the help of SPSS v16 program.

RESULTS

Table 1 shows the baseline and day 10 Mean and Standard Deviation data.

Table 1. Baseline and 10 days mean and SD

Group		N	Minimum	Maximum	Mean	Std. Deviation
1 Treatment	WT1	48	56.0	123.0	79.563	15.9533
	WT10	48	55.0	120.0	78.056	15.3782
	ABD1	47	75.0	135.0	97.723	13.5626
	ABD10	46	71.0	126.0	92.946	12.1336
	Hip1	47	86.0	127.0	105.447	9.2450
	Hip10	47	81.0	125.0	103.830	9.6077
	SBP1	48	92	200	133.79	21.382
	SBP10	47	95	156	116.57	14.423
	DBP1	48	60	110	81.31	11.329
	DBP10	47	58	90	72.74	8.292
	BS1 Baseline Blood Sugar	47	76.4	216.0	105.862	25.6266
	BS10 10-day Blood Sugar	47	63.5	141.2	80.034	14.8410
	CHOL1	48	152.4	341.0	237.655	46.4351
	Chol10	47	105.6	240.0	164.015	32.4950
	TG1	48	55.0	275.0	120.037	56.4284
	TG10	47	37.1	289.2	96.690	53.1316
	HDL1	48	37.1	110.9	55.283	13.1836
	HDL10	47	27.4	55.1	40.528	7.0807
	LDL1	48	93.0	231.2	158.365	37.7368
	LDL10	47	54.9	157.0	104.149	24.5780
	BMI1	48	19.96	41.10	29.0692	4.95352
	BMI10	48	20.31	40.09	28.5219	4.75995
	Valid N (listwise)	45				
2 Control	WT1	49	43.0	119.0	79.539	14.8740
	WT10	49	48.0	117.4	79.702	14.7596
	ABD1	49	72.0	118.0	93.347	10.7482
	ABD10	48	68.5	118.0	93.500	12.2713
	Hip1	49	88.0	127.0	105.551	9.4914

Hip10	48	90.0	128.0	104.885	8.8692
SBP1	49	78	190	140.24	21.170
SBP10	48	92	173	128.40	17.261
DBP1	49	50	114	87.24	12.070
DBP10	48	50	100	78.19	10.418
BS1 Baseline Blood Sugar	49	84.0	130.0	100.163	8.4640
BS10 10-day Blood Sugar	48	64.6	112.5	82.787	10.3363
CHOL1	48	141.9	349.0	236.579	47.0398
Chol10	47	111.0	273.8	199.378	37.5869
TG1	48	54.0	315.0	134.875	65.8279
TG10	47	34.3	214.5	89.191	43.0899
HDL1	48	33.6	114.0	58.301	14.8108
HDL10	47	32.4	99.0	52.961	12.1343
LDL1	48	56.8	239.4	151.303	39.3151
LDL10	47	53.5	195.1	128.579	33.3947
BMI1	49	20.76	40.58	28.6013	4.42493
BMI10	49	21.11	40.35	28.6651	4.34489
Valid N (listwise)	47				

(WT=weight, ABD=abdominal circumference, Hip=hip circumference, SBP=systolic blood pressure, DBP=diastolic blood pressure, CHOL=total cholesterol, TG=triglycerides)

Table 2 presents paired T test for the Treatment group with the corresponding p values being all statistically significant $p<0.05$. Table 3 presents paired T test for the Control group with mixed results concerning the p value (some statistically significant changes occurs also in this group).

Table 2. Paired T test – Treatment group (day 10 –baseline)

Treatment

Pair	**Mean**	Std. Deviation	95% Confidence Interval of the Difference		**P-value**
WT10 - WT1	-1.5063	1.5918	-1.9685	-1.0440	.000
ABD10 - ABD1	-4.7444	4.6620	-6.1451	-3.3438	.000
Hip10 - Hip1	-1.3913	3.1215	-2.3183	-.4643	.004
SBP10 - SBP1	-17.511	19.439	-23.218	-11.803	.000
DBP10 - DBP1	-8.809	11.218	-12.102	-5.515	.000
10-day Blood Sugar - Baseline Blood Sugar	-25.8277	22.6100	-32.4662	-19.1891	.000
Chol10 - CHOL1	-73.1438	28.0426	-81.3774	-64.9102	.000
TG10 - TG1	-20.2417	47.0732	-34.0629	-6.4205	*.005*
HDL10 - HDL1	-15.0383	9.1717	-17.7312	-12.3454	.000
LDL10 - LDL1	-54.0572	23.5830	-60.9814	-47.1330	.000
BMI10 - BMI1	-.54732	.54344	-.70512	-.38953	.000

Table 3. Paired T test – Control group (day 10 –baseline)

Pair	**Mean**	Std. Deviation	95% Confidence Interval of the Difference		**P-value**
WT10 - WT1	.1633	1.6866	-.3212	.6477	.501
ABD10 - ABD1	.5000	4.5535	-.8222	1.8222	.451
Hip10 - Hip1	-.2396	3.3166	-1.2026	.7235	.619
SBP10 - SBP1	-11.854	17.678	-16.987	-6.721	.000
DBP10 - DBP1	-9.000	12.476	-12.623	-5.377	.000
10-day Blood Sugar - Baseline Blood Sugar	-17.4008	7.6034	-19.6086	-15.1930	.000
Chol10 - CHOL1	-37.6457	20.9725	-43.8035	-31.4880	.000

TG10 - TG1	-44.0540	36.3107	-54.7153	-33.3928	.000
HDL10 - HDL1	-5.7083	5.6563	-7.3691	-4.0475	.000
LDL10 - LDL1	-23.1266	18.9921	-28.7029	-17.5504	.000
BMI10 - BMI1	.06375	.65306			.498

In Figures 1 to 11 we have the graphic description of mean values changes occurred after the 10 day. The Treatment group has been the object of our intervention while the Control group went about their normal working program and usual care.

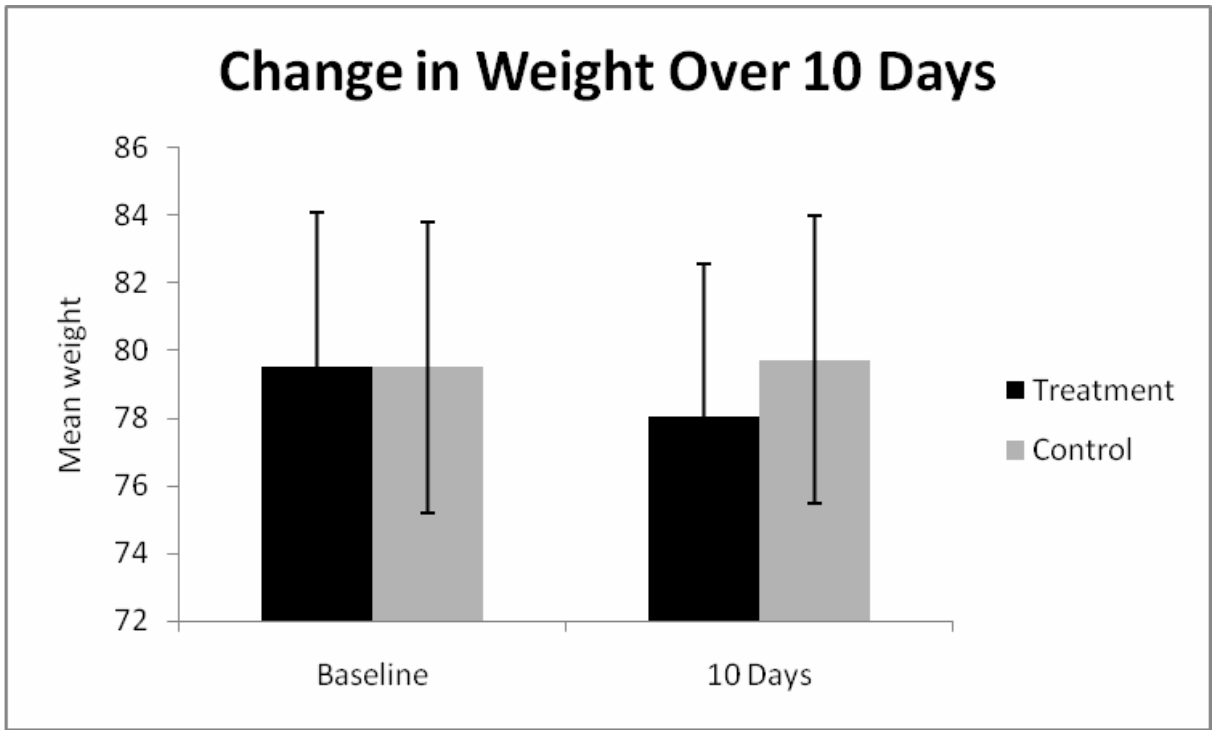

Figure 1. Weight

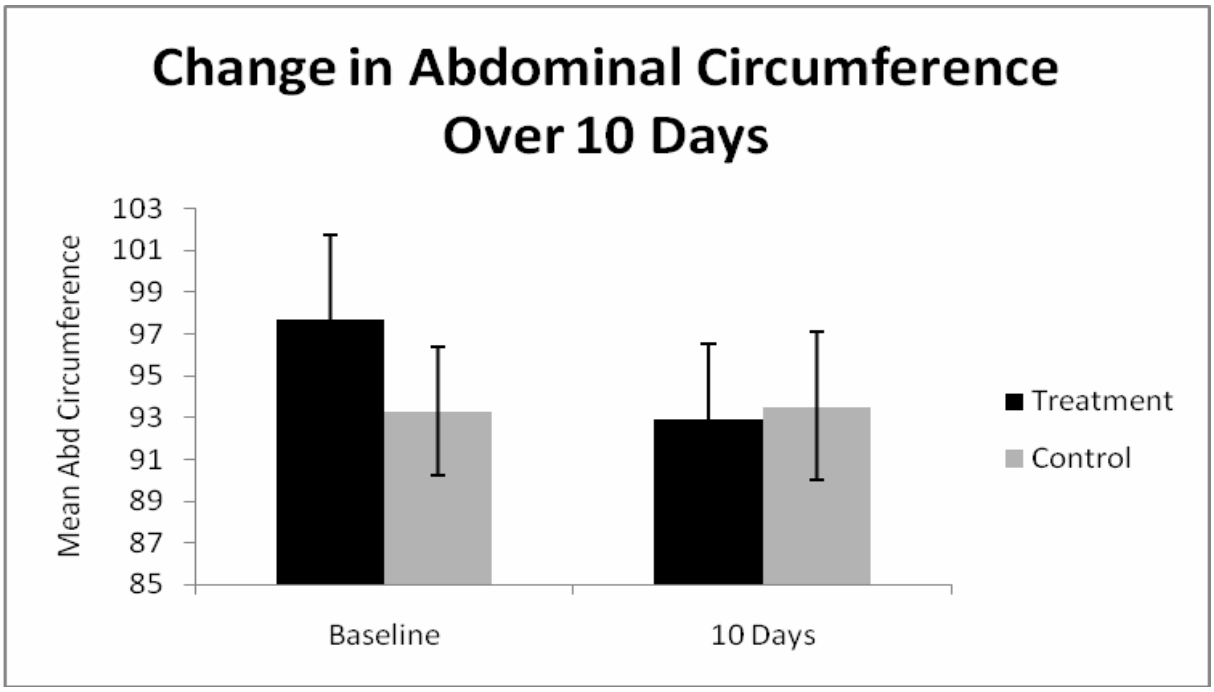

Figure 2. Abdominal circumference

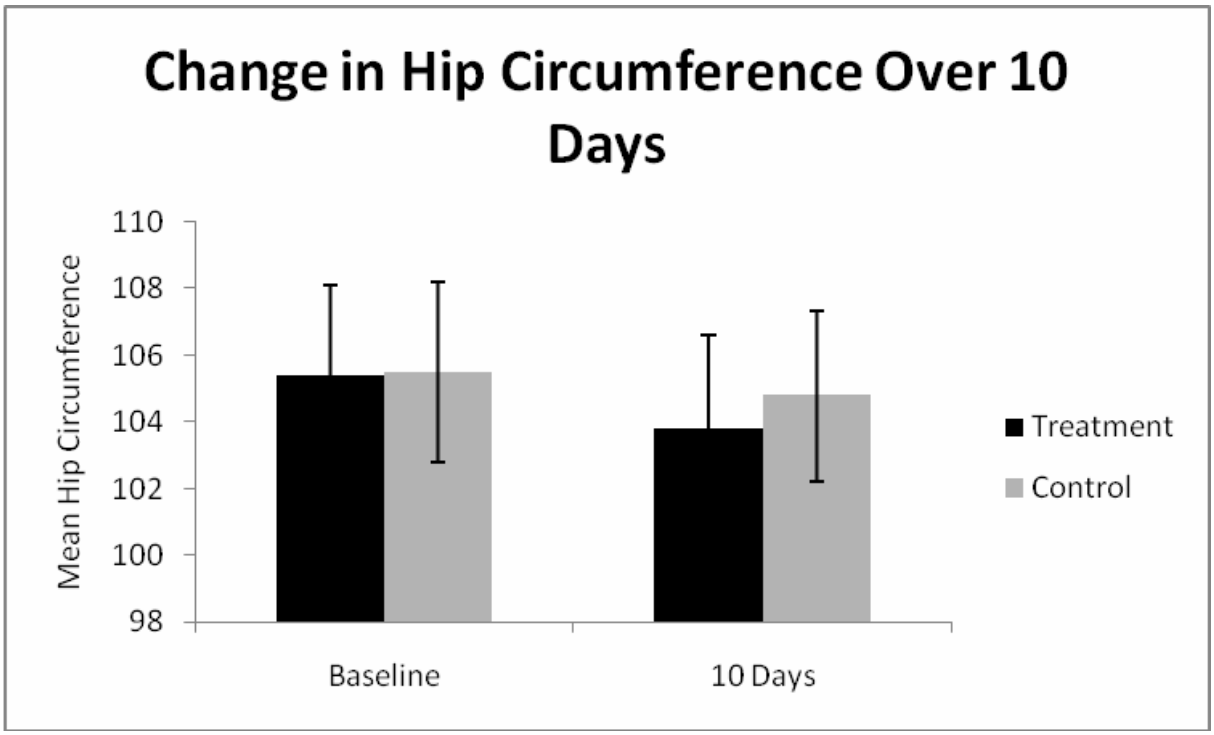

Figure 3. Hip circumference

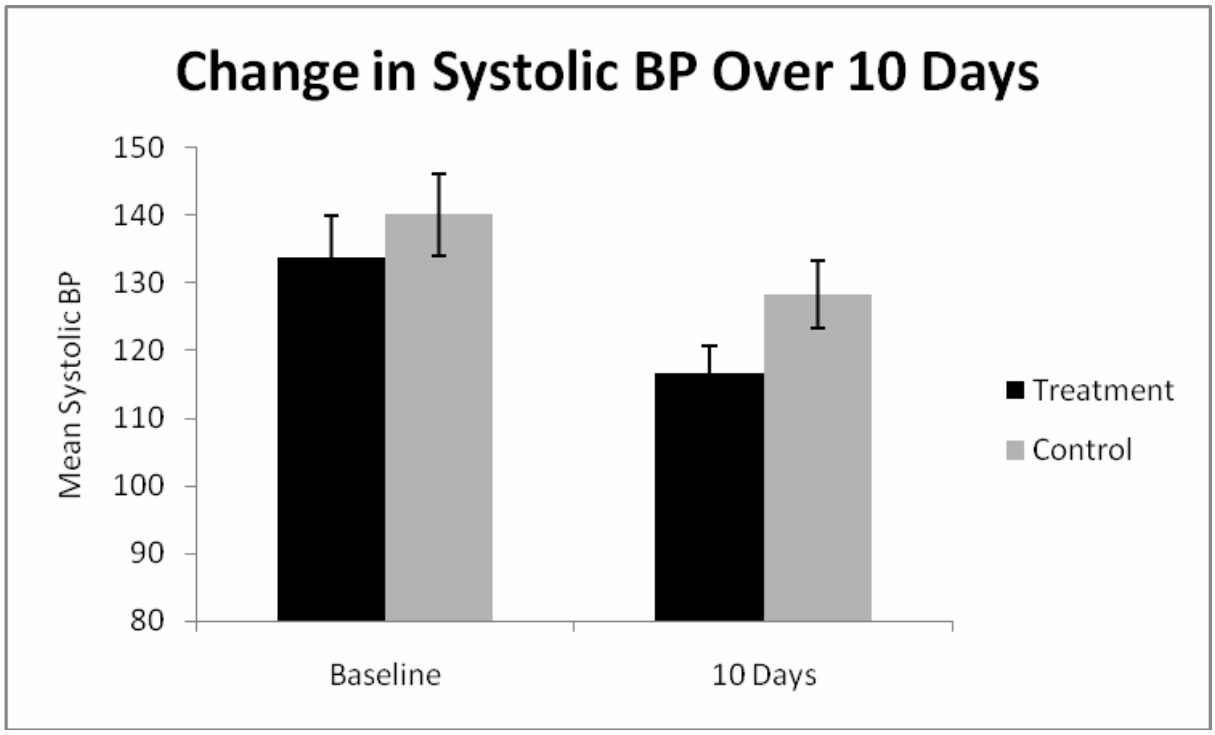

Figure 4. Systolic Blood Pressure

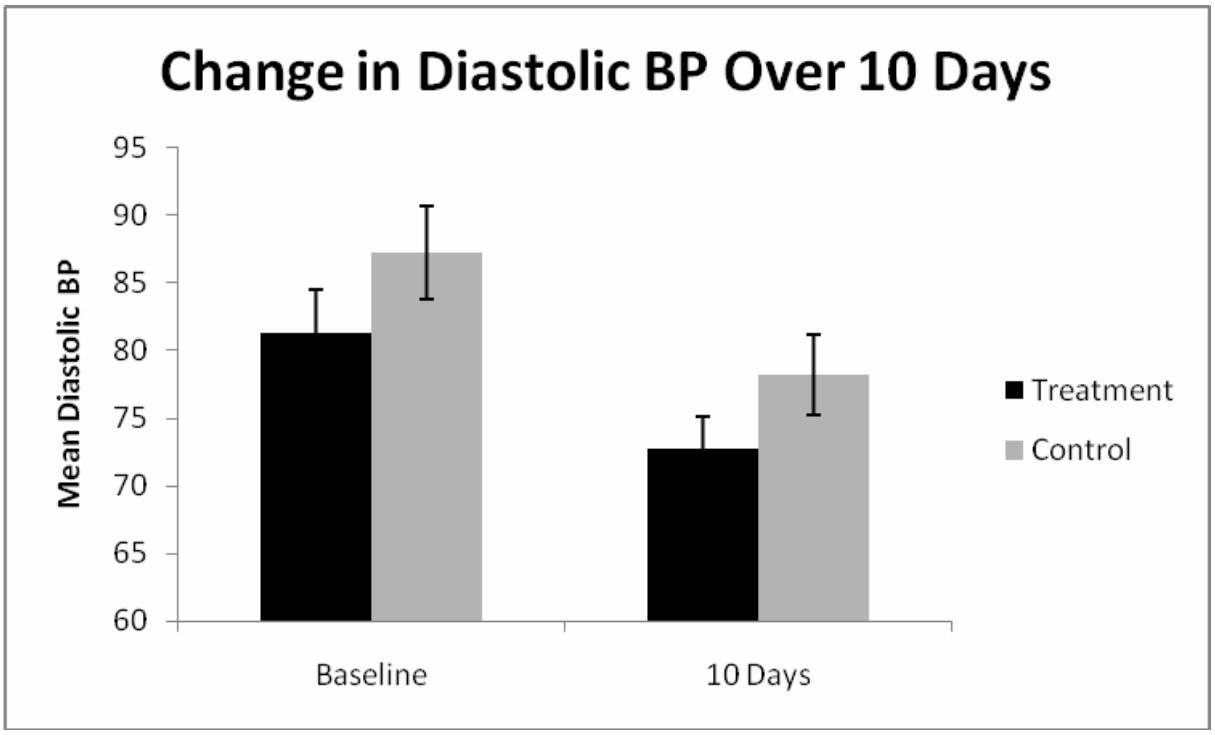

Figure 5. Diastolic Blood Pressure

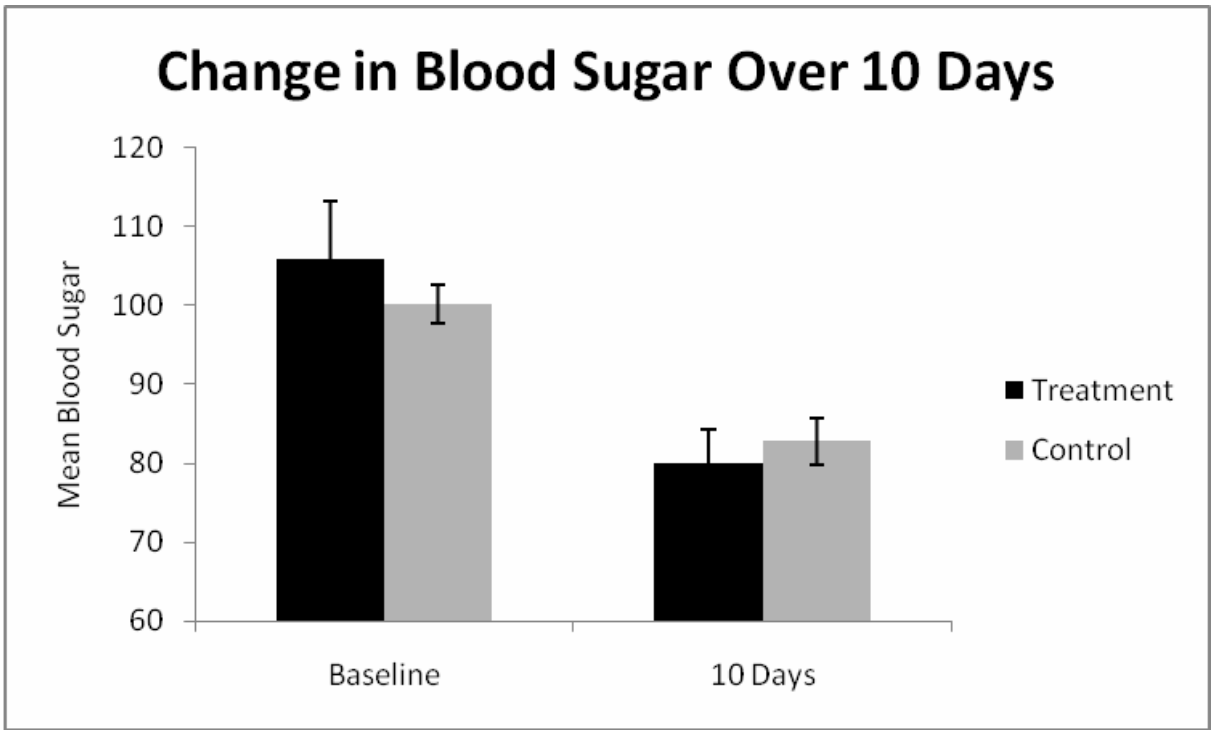

Figure 6. Blood sugar

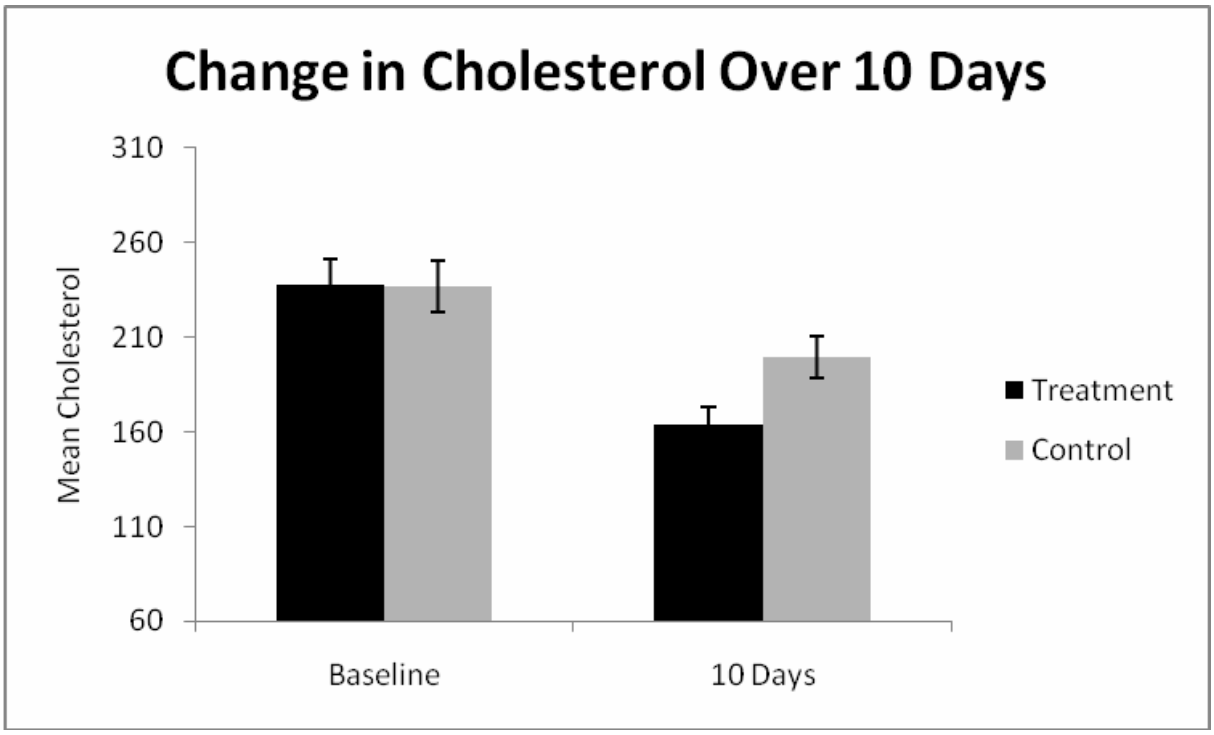

Figure 7. Total Cholesterol

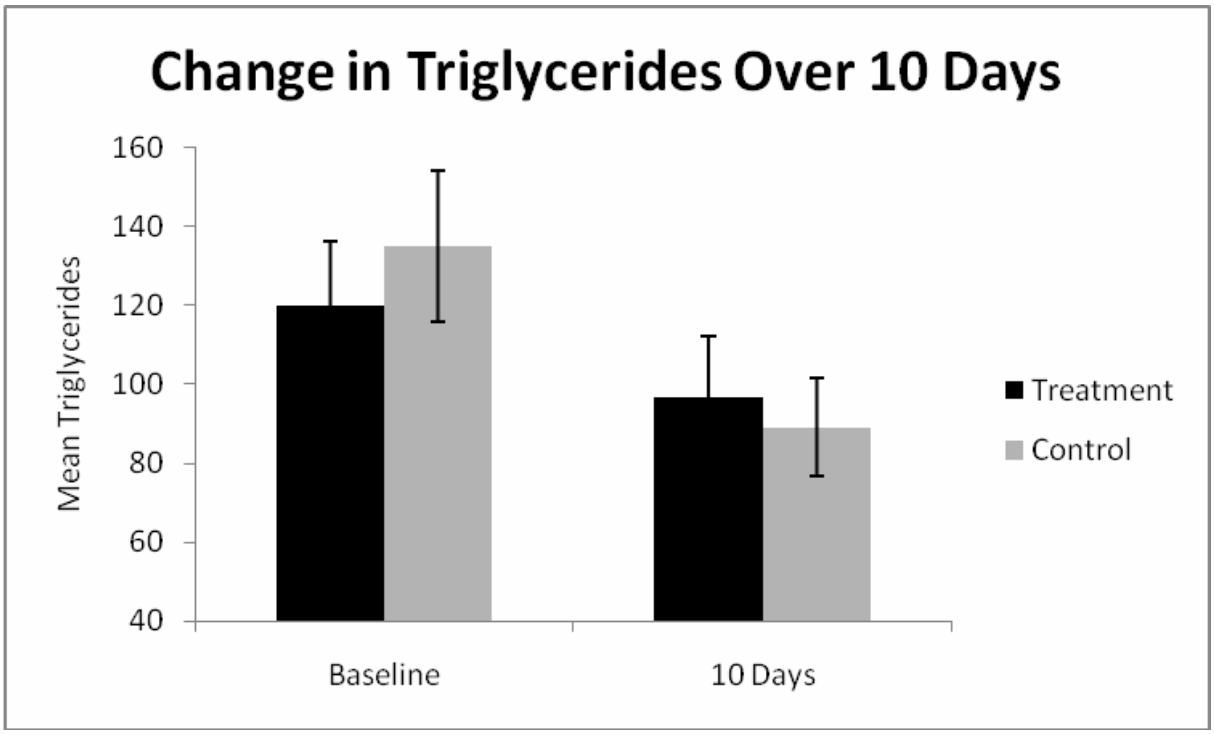

Figure 8. Triglycerides

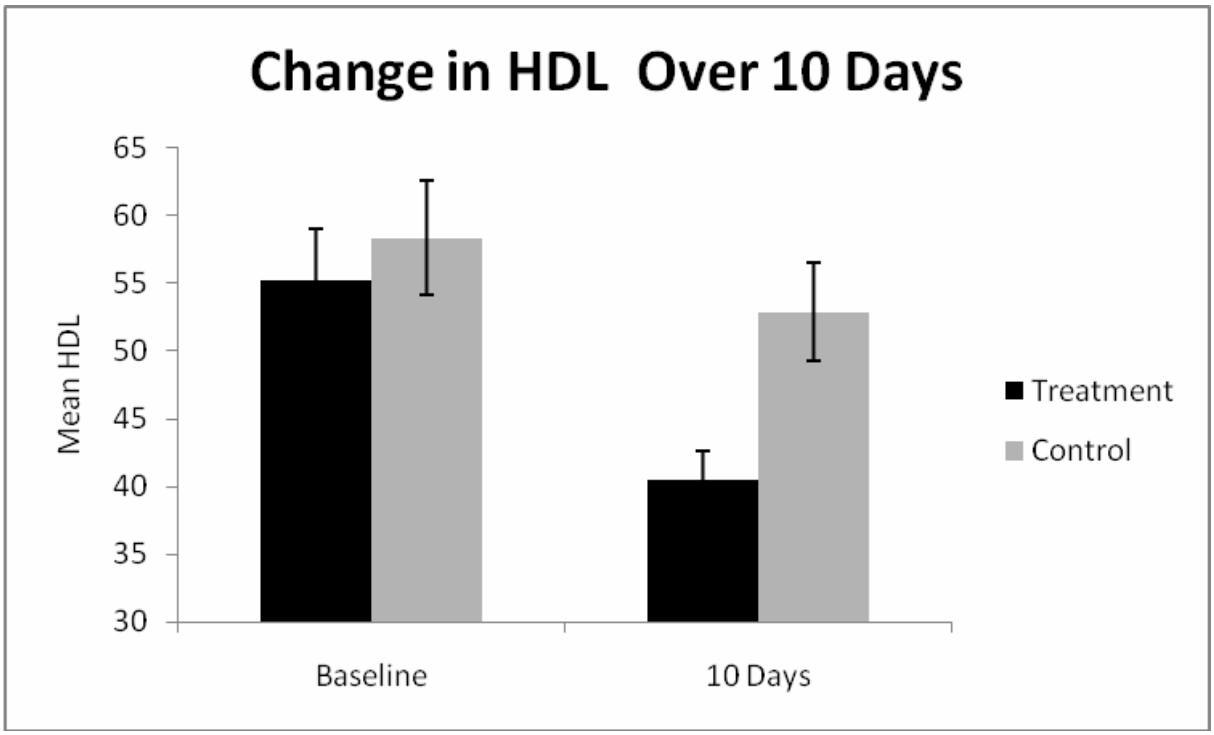

Figure 9. HDL - Cholesterol

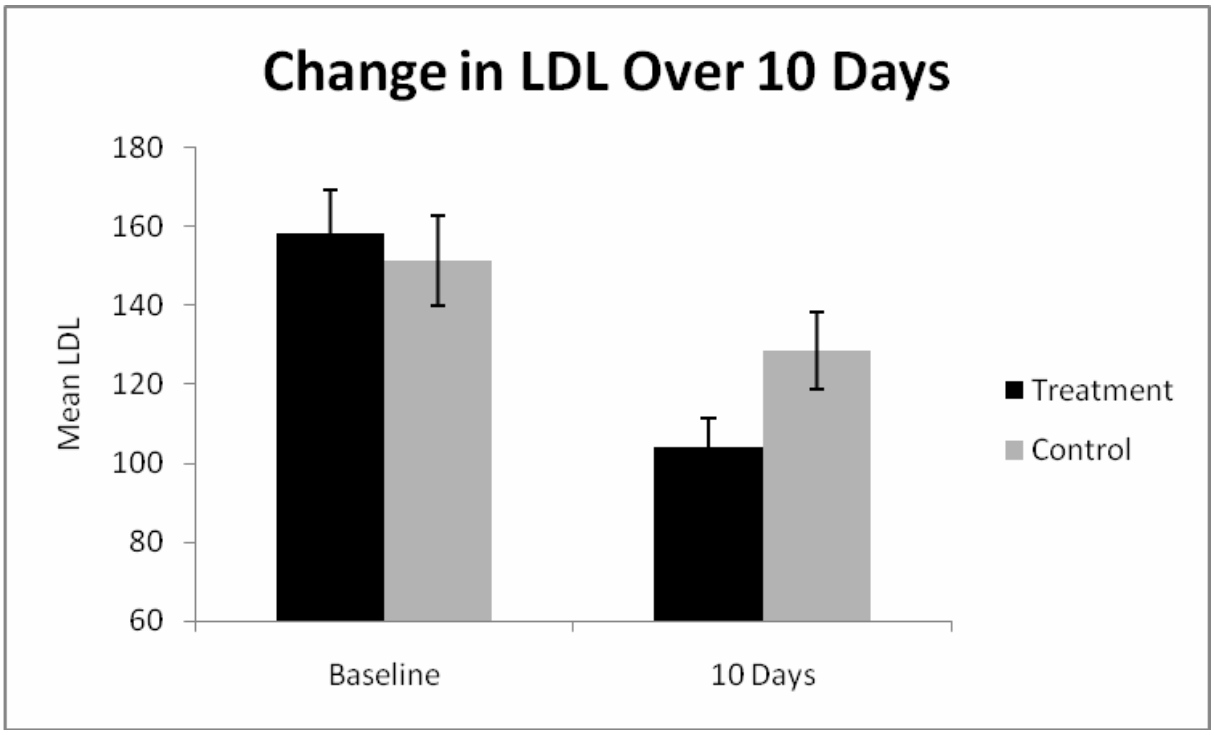

Figure 10. LDL - Cholesterol

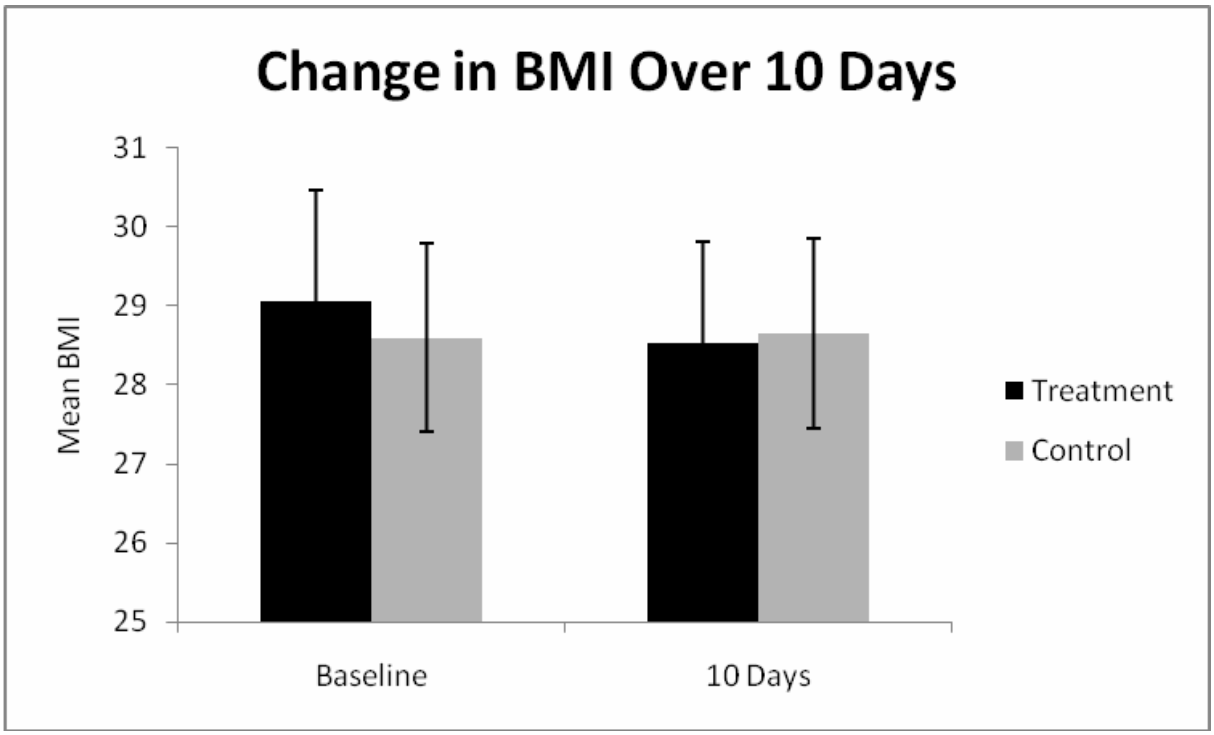

Figure 11. Body Mass Index

After 10 days there was statistically significant difference between the two groups (Independent t test, $p< 0.05$) as far as: total cholesterol ($p<0.001$) - in the treatment group the blood cholesterol decrease with 31%; LDL-cholesterol($p<0.001$) - in the treatment group LDL-cholesterol decreased with 34%;

glycemia ($p<0.018$) – in the treatment group glycemia decreased on average with 26mg/dl; body weight ($p<0.001$) – in the treatment group the weight decreased with an average of 1.6 kg; abdominal circumference ($p<0.001$) – in the treatment group the average drop was 5 cm; BMI with the $p<0.001$.

Triglycerides dropped statistically significant within both groups but there was no difference when we compared the two groups. Blood pressure both SBP and DBP dropped significantly in both groups but when we compared one against the other there was no statistical difference between them ($p>0.05$).

DISCUSSION

The first objective of our Herghelia Lifestyle Study was to find out whether the outstanding results obtain in our program over 13 years are not exaggerated or biased by potential hand picking and/ self-selection biases. Our study seems to confirm that major changes in the profile of CHD risk factors may be achieved in a relatively short period of time, as it is in our 11 day program at Herghelia, regardless the target group. The null hypothesis seems to be invalidated by our results but of course other studies of similar programs needs to bring more evidences.

The results were achieved through significant lifestyle improvements, and without registering the slightest side effects, and it seems that these changes may contribute decisively to lower the risk and improving the clinical outlook of conditions like: CHD, diabetes, obesity, dyslipidemia etc. The decrease of the blood cholesterol value is quite impressive - 31% in just 10 days and this in the context of the healthy worker effect. It is true, the decrease might be due to the period of the year when we conducted the study, it was immediately after the Christmas and New Year holydays. It may be that during this holiday season people eat a diet rich in animal fat and concentrated sweets and are more sedentary leading to an increase in blood cholesterol beyond their average value. Also, in the Control group the total cholesterol dropped an average of 15% but because they started from the same value, and the Treatment group had an additional drop of 16% there was a highly statistically significant difference between the two groups.

The HDL seems to be somehow a surprise because we would expect that in the context of a healthy lifestyle it will go up, reflecting an improved lipid profile. There were controversies in the literature over this issue back in the 90's when Dean Ornish published in Lancet The Lifestyle Heart Trial. He showed similar results in a randomized lifestyle trial done in previously diagnosed CHD patients, and the HDL went initially down, too. When we have major drops of the Total blood cholesterol it is expected that the HDL-cholesterol will drop, too. LDL and HDL are part of the total cholesterol value and it is expected when registering massive and rapid change in total cholesterol and LDL-cholesterol to see drops in HDL cholesterol. In fact, we should rather look at the change of the C-T/HDL ratio which according with the risk equations derived from the Framingham Study is predictive of CHD risk (when the value of the ratio is 3.4 signifies just 50% of average risk; 5.1 means average risk; 6.8 means doubled risk and 7.8 signify tripled risk – for men and for women the corresponding values are 2.5; 4.4; 6.4 and 7.5). In the Treatment group the C-T/HDL ratio went from 4.2 at baseline to 4 at day 10 and went down to 3.4 in the 45th day of the study which reflects a decrease of the risk for CHD despite the decrease in HDL. The Control group also had this ratio decrease from 4 to 3.75 by day 10 and to 3.37 by day 45. There is no data showing that a decrease of the HDL in the framework of a low fat diet is detrimental to health or increase the risk for disease.

A reduced HDL induced by a low fat, high complex carbohydrates diet does not confer same CHD risk in Americans like a reduced level of HDL due to high fat diet consumption.

The drop in HDL cholesterol by eating a low fat diet results in an increased HDL clearance and a decrease of the HDL apo-protein transport. Populations with a habitual low fat diet who have a decreased HDL don't show an increase in CHD.
It is a known fact that:

- Stop smoking decrease the risk for myocardial infarct (MI) between 50-75% in 5 years
- Decreasing cholesterol by 1% we decrease the risk for MI with 2-3%
- Exercising regularly decrease the risk for MI with 45%
- Decreasing the weight to a healthy weight in obese people decrease the risk for MI with 35-55%
- Reducing the blood pressure with 1mmHg will decrease the risk for MI with 2-3%

Thus the results obtained at Herghelia Lifestyle Center in a relative short time can have an impact comparable or even better than that obtained through drug approaches only, if the lifestyle changes may be maintained over time, as demonstrated in The Lifestyle Heart Trial where the patients in the Treatment group maintained the positive gains at the 5 year check up. The Herghelia Lifestyle Study suggest the possibility to use lifestyle therapies not only for prevention purposes but also as part of the therapeutic plan for fighting chronic diseases like CHD, diabetes and obesity.

CONCLUSION

The Herghelia Lifestyle Study and data accumulated over 13 years of experience at Herghelia Lifestyle Center show that:
1. The lifestyle change program at Herghelia (including a plant based diet) seem to have the same positive results in a general working population like the results obtained by the patients coming voluntarily to our program. A major reduction in the major CHD risk factors may be obtained through a multi-factorial lifestyle intervention in a relatively short period of time, in the general working population.
2. The inference that the noteworthy results obtained in a residential lifestyle change program might be attributed to self-selection and hand-picking bias seems to be invalidated by our results. Our study suggests that the results obtain at Herghelia during the past 13 years of activity might be applied also to the general population (or at least to the general working population) and particularly to those of them having a high risk for/or those already having: CHD, diabetes and obesity. The results obtained at Herghelia Lifestyle Center offer food for thought regarding the need of placing a bigger emphasis on the behavioral change interventions focused on behaviors which place a major proportion of Romania's population at risk for cardiovascular diseases, diabetes and obesity.
3. While for a smaller fraction of the population might be proper a drastic diet like the therapeutic one served at Herghelia, we need to propose for the majority of the population more realistic diets, somewhere between 24% and 30% calories coming from fat (however, from 24% down we can speak about regression of atherosclerosis in case of those with CHD, at 30% the atherosclerotic plaque is progressing still!)
4. Diet plays an important role in: atherogenesis, in the interplay of blood lipids and lipids handling enzymes like LPL, in the obesity gene modeling, in the glucose intolerance and insulin resistance. According with the Interheart Study, regardless geography and ethnicity 50% of MI can be attributed to diet (that is half of all MI). The rest of 40% are due to exercise and other lifestyle modulated variable with only 10% of the risk factors being non-modifiable. For all these reason a Herghelia type diet might be an important key to

reduce significantly the risk factors for CHD thus reducing the risk for major coronary events. While the Herghelia diet is quite restrictive it might be beneficial for a large part of the population at risk for CHD.

I will end with a fitting thought spoken long before by Alfred Whitehead: „Familiar things happen and mankind does not bother about them. It requires a very unusual mind to undertake the analysis of the obvious." The almost universally popular knowledge that there is a strong link between our lifestyle (and particularly our diet) and a host of chronic disease including CHD is probably one of those familiar things often forgotten and overlooked.

REFERENCES

1.***, http://www.clon.ro/stiri/cluj/articol/140000-de-clujeni-risca-sa-se-238mbolnaveasca-de-diabet-zaharat/cn/news-20081202-10574843 accesat la 26/05/2009

2. ***, European Summit on CVD Prevention - Call for Action: To promote a heart healthy environment in Europe. http://www.escardio.org/Policy/prevention/initiatives/european-summit/Documents/eusummit2008-call-action.pdf accesat 12/24/2008 11:12 AM

3. ***, 2006, Preventing Cardiovascular Disease and Diabetes. A Call to Action From the American Diabetes Association and the American Heart Association. Circulation. 2006;113:2943-2946. 2006 American Heart Association, Inc.

4. ***, 2002, Global approach to health initiatives of importance for the prevention of cardiovascular disease The European Society of Cardiology and the World Heart Federation Joint Session. Dr. Derek Yach, WHO director non-communicable diseases. Sunday, 1 September 2002

5. Ornish D. et al., 1990, Can lifestyle changes reverse coronary heart disease? The Lifestyle Heart Trial. Lancet 1990; 336:129-33.

6. Connor and Connor, Katan, Grundy, Willet. Should a Low-Fat, High-Carbohydrate Diet Be Recommended for Everyone? Clinical Debate. NEJM, August 21, 1997, Number 8Volume 337:562-567

7. Brinton E.A., Eisenberg S., Breslow J.L., 1990, A low-fat diet decreases high density lipoprotein (HDL) cholesterol levels by decreasing HDL apolipo-protein transport rates. J Clin Invest 1990;85:144-151.

8. Connor W.E., Cerqueira M.T., Connor R.W., Wallace R.B., Malinow M.R., Casdorph H.R., 1978, The plasma lipids, lipoproteins, and diet of the Tarahumara Indians of Mexico. Am J Clin Nutr 1978;31:1131-1142.
9. Knuiman J.T., West C.E., Burema J., 1982, Serum total and high density lipoprotein cholesterol concentrations and body mass index in adult men from 13 countries. Am J Epidemiol 1982;116:631-642.
10. Nedley N. 1999, Proof Positive, N&N Publishing, p 83
11. Barbard N. 2001, Turn Off the Fat Genes, p12
12. Salim Y. at al., 2004, Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study). Lancet 2004; 264:937-52
13. Whitehead, Alfred North, 1925, Science and the Modern World. New York: Macmillan.

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SHOULD PHYSICIANS CONCEAL CERTAIN TREATMENT OPTIONS FROM THEIR PATIENTS JUST BECAUSE THEY ARE COMPLEX? SHOULD PHYSICIANS BE THE ONLY DECIDER CONCERNING THE BEST TREATMENT OPTION FOR THEIR PATIENTS? PRACTICAL PUBLIC HEALTH ISSUES DRAW FROM HERGHELIA LIFESTYLE STUDY DATA

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REZUMAT

Există o abundenţă de date ştiinţifice incluzând şi cele provenite de la trialul Herghelia Lifestyle Study care indică faptul că expertiza în următoarele domenii: schimbarea stilului de viaţă şi a comportamentului, Educaţie pentru Sănătate şi Promovarea Sănătăţii, Sănătate Publică (atât cunoştinţe cât şi viziune) ar trebui să devină parte integrantă a pregătirii medicale a viitoarelor generaţii de medici care se confruntă cu o creştere fără precedent a ratelor obezităţii, diabetului şi a bolilor cardiovasculare. Conform noii gândiri în ce priveşte pregătire medicală va fi obligatoriu pentru viitorii medici să aibă viziunea Sănătăţii Publice în timp ce vor practica o îngrijirea a pacienţilor focalizată pe prevenţie. Intervenţiile în zona schimbării comportamentului şi a stilului de viaţă sunt inevitabil legate de confruntare cu bolile cronice şi în speţă cu bolile coronare. În esenţă este vorba de nevoia unui proces educaţional prin care pacienţii înţeleg fiziologia propriului organism şi importanţa alinierii comportamentului la legile fiziologiei iar medicii învaţă metode de schimbare a comportamentului şi a stilului de viaţă care vor ajuta pacienţii să îmbrăţişeze un stil de viaţă dictat de legile fiziologiei şi nu de capriciile obiceiurilor nesănătoase.

***Cuvite cheie**: stil de viaţă, schimbări comportamentale, boli coronare, pregătire medicală, etică*

ABSTRACT

There is wealth of data including our new data coming from Herghelia Lifestyle Study indicating that lifestyle change and behavioral modification expertise, Health Education and Promotion and getting Public Health vision and knowledge should be part and parcel of medical training for the new generations of physicians facing an unprecedented rise in obesity, cardio-vascular disease and diabetes. According with the new paradigm shift about medical education it will be mandatory for future physicians to have Public Health and Prevention vision while practicing prevention oriented patient care. Interventions in the area of behavior and lifestyle change are inevitably involved in the battle with all chronic disease and particularly with CHD. Essentially, we are talking about the need of an educational process in which patients understand the physiology of their own body and the importance to align their behavior with its laws and physicians learn behavior and lifestyle change methods which are helping patients to embrace a lifestyle dictated by the law of physiology and not by the whim of unhealthy habits.

***Keywords**: Lifestyle, behavior change, CHD, medical training, ethic*

As noted in the articles published in this issue of the journal the positive findings resulted from Herghelia Lifestyle Study converge with the results obtained on almost every group of 40-50 people who come to Herghelia every two weeks for a session. The results of the lifestyle intervention in CHD are impressive, at least as impressive as the latest drug intervention, with the added benefits of no side effects and maybe less expenses for the family budget.

When we compared the outcome at 10 days against the baseline in the Treatment group (paired T test), all variables measured (TC, LDL, HDL, TG, glycemia, abdominal and hip circumference, weight, SBP and DBP, and BMI) where statistical highly significantly lower/improved.

After 10 days there was also statistically significant difference between the two groups for: total cholesterol ($p<0.001$) - in the treatment group the blood cholesterol decrease with 31%; LDL-cholesterol ($p<0.001$) - in the treatment group LDL-cholesterol decreased with 34%; glycemia ($p<0,018$) – in the treatment group glycemia decreased on average with 26mg/dl; body weight ($p<0.001$) – in the treatment group the weight decreased with an average of 1.6 kg; abdominal circumference ($p<0.001$) – in the treatment group the average drop was 5 cm; BMI with the $p<0.001$. Triglycerides drooped statistically significant within both groups but there was no difference when we compared the two groups. Blood pressure both SBP and DBP dropped significantly again in both groups but when we compared one against the other there was no statistical difference between them ($p>0.05$).

The question when seeing this magnitude of change is obvious: is it possible to extend these results to the general population translating them into general recommendations and guides? If the answer is yes what would be the consequences and if the answer is no what would we lose?

Lifestyle change is and will be always a challenge, even for medical professionals.
Commenting about the attitude of many physicians Dr. Dean Ornish, professor of medicine at the UC San Francisco once said: "It is a very paternalistic attitude to say, 'We know you won't even do it because it's hard.'…The (lifestyle) program is not for everyone, but there is a larger percentage of people interested in following a program like this than many doctors might believe… I don't understand why asking people to eat

a well-balanced plant based diet is considered drastic, while it is 'medically conservative' to cut people (hearts) open and put them on cholesterol-lowering drugs for the rest of their lives." Likewise, we could say the same thing concerning many others healthy behaviors: it is not feasible for the XXI century pace to put people on a regular exercise program, or asking them to eat daily a good breakfast, or to sleep 7-8 hours a night; we (physicians) should not ask people to do these because they won't do it.

The familiar mantra of most medical professionals when coming to implementing lifestyle change in a clinical setting is that low fat diet, daily exercise, eating regularly a consistent breakfast are not feasible that's why we should put them on medication and hope they will still stick to it after 2-3 months, although current research shows that people are not more consistent in taking medication á la long then in making lifestyle change á la long. Studies have shown that just 1/3 of the heart disease patients follow their physicians' advice in dealing with: high cholesterol, high blood pressure, lack of exercise and smoking. Incidentally, all these behaviors valuable in preventing and treating CHD seem to be the hallmark of successful maintenance of weight loss (and weight is closely correlated with the risk for diabetes type II). Therefore we are discouraging important behaviors affecting potentially the risk factors for an estimated 60-70% of all cause of death in Romania. In an article published in 2005 by Hill JO et al in the Journal of Nutrition Education and Behavior the researchers comment that:" The National Weight Control Registry (NWCR) consists of over 4800 individuals who have been successful in long-term weight loss maintenance. The purpose of establishing the NWCR was to identify the common characteristics of those who succeed in long-term weight loss maintenance. We found very little similarity in how these individuals lost weight but (we found) some common behaviors in how they are keeping their weight off. To maintain their weight loss NWCR participants report eating a relatively low-fat diet, eating breakfast almost every day, weighing themselves regularly, and engaging in high levels (about 1 hour/day) of physical activity."

I believe that by not telling people what they should do albeit that is not the easy road, when we know what the research is telling us; and by not telling patients that there is hope, there is an ideal treatment for obesity or for CHD (even if they already take drugs for the lately) we might run into ethical issues.

Lifestyle, medication and ethical issues

It is ethical for a physician consulting and treating a patient to tell him or her all the option, and by the same token it is not ethical (even if it is very frequently done) not to tell patients all the options and to choose (instead letting the patients to choose) to arbitrary leave out some options just because we suppose will be difficult for them to follow those options.

It was a time in the first part of XXth century when physicians in western countries didn't know yet that smoking is dangerous for your health. There were some who even prescribed smoking for certain respiratory conditions. In the same time there were visionary physicians and health advocates who said smoking is poisonous. Those singular voices were not able to curb the use of tobacco which in fact increased in the first part of the century because the majority of physicians didn't think smoking is bad. Time passed, research showed the true face of smoking, in 1964 The Surgeon General's Report on Smoking and Health was a breakthrough and little by little physicians began to tell patients smoking is deleterious to health. Smoking rates went down in the second half of the century (specially after 70') and I imagine that this could have not happen if we would have done all other things like forbid billboards

and advertising, not sell to teenagers etc. except the voice of physicians. When physicians are not on board patients will do little to change long cherished habits.

Suppose a physician sees a patient with a rare but dangerous disease and he knows there is a cure for that disease but the medication is very expensive. Will be ethical for the physician to withhold that information about the drug because he supposes the patient will not have the means to purchase it? Does it happen like that? Not really – physician don't hesitate to tell patients about a better drug (a better statin, a better beta-blocker) or much more about an ideal drug even if it is expensive and/or need to be purchased from oversees. Why then physicians do not realize that is wholly unethical to withhold information from the patients just because we - the physicians together with the pharmaceutical industry, made already the decision for the poor patient: because is too hard for the patients to change their lifestyle concerning eating habits and exercise we won't tell them about this option because they won't do it, so we will give them drugs. I believe in many of these instances the handling of patients is unethical and probably physicians should be held accountable when withholding information concerning all options for treatment.

Is it possible to implement multi-factorial lifestyle change programs at population level?

Herghelia Lifestyle Study appears to validate the outstanding results obtained in the population subgroup of patients coming at Herghelia over the last 13 years (over 10,000 cases) as applicable to the rest of the population, at least to the working people regardless of age. The puzzling question is: how could we implement multi-factorial lifestyle change programs, similar to the one at Herghelia Lifestyle Center, at the level of general population. Such an effort paid off for Finland, when a county (North-Karelia) was selected where such a program was conducted, and as a result, by contamination from county to county, Finland is today not anymore a leader in cardiovascular mortality in Europe but it's a leader in prevention. KTL (National Public Health Institute of Finland) is now considered one of the best national health institutes in Europe. Professor Pekka Puska, the young and idealistic then Public Health physician (it was in early 70' when the Karelia Project began) started small with health lectures at the local Old Ladies' Clubs, then he went on television and radio stations and began to work with family physicians at a time when KTL had 3 employees in a small office for Chronic Disease Prevention.. As physicians rallied and the health education and promotion gained momentum while the food industry diversified the health food offer things changed dramatically in North Karelia. When they started Karelia Project the proportion of smoker in North Karelia County was 52% (age group 25-59), the average blood cholesterol was 270ml/dl, and average blood pressure count was 150/92 mm Hg with 34% of people having a SBP over 95mmHg. In an article published by prof. Puska in 2002 he has shown that Karelia Project became a demonstrational project for all the rest of Finland "contaminating" county after county. In 25 years the percentage of smokers dropped to 31%. Before the project started people in Finland would rarely eat vegetables and vegetable oil and 90% of the population used almost exclusively butter on bread. After 25 years vegetables and vegetable oil are common staples and only 7% of the population use exclusively butter on bread. The total cholesterol dropped accordingly on average with 17%. Raised Blood Pressure has been brought down under control and physical exercise increased. In 25 years the annual mortality rate through CHD in male adult population dropped 73%, mortality by pulmonary cancer dropped 70% in Karelia and 60% in Finland. General mortality dropped 45% increasing the lifespan with 7 years for men and 6 years for women.

An independent investigation has shown that the decrease in the mortality by CHD could be mainly explained through change in the risk factors profile (lifestyle change) and that the decrease in blood cholesterol has been the biggest contributor to the positive outcome.

Today KTL has over 400 employees in the Department of Chronic Disease Prevention and is a hub of research known in the entire world. Incidentally Prof. Pekka Puska is the general director of KTL. This success story gives hope that taking the findings of our study to the general population is possible but not easy.

Why is so hard to copy Karelia model?

In an excellent article published by Harlan and Strosss in JAMA they analyzed the need of a collaborative effort between Public Health and the usual internal and cardiology medical care sector for the prevention of CHD. They analyzed the collaboration between National High Blood Pressure Education Program and the American Heart Association for the National Campaign for Controlling Hypertension in USA between 1960 and 1980 and noted the fact that The National Cholesterol Education Program to prevent CHD needed to be undertaken with a totally different educational approach.

The Campaign for Controlling Hypertension like many other successful Public Health education programs had a very straightforward educational message leading to simple behaviors: measure annually your blood pressure; if high, seek treatment from your physician; if treated maintain habitually the treatment. The intervention in patient's lifestyle was minimal. The results were quick and visible. By contrast, in The National Cholesterol Education Program, lifestyle related to eating and exercise habits needed to be clearly changed, because there were no evidences that the drug therapy should be used preventively on a large scale. From the beginning of last decade we knew from Oslo Study that there is possible to change significantly the eating behavior of middle age men with high risk for CHD, with relatively modest effort (specially if the family is also included in the educational effort). Overall the changes obtained in this study were translated into a significant drop of the blood cholesterol which in turn influenced a statistically significant reduction of 46% for the coronary acute events.

However, the majority of physician is not capable to use a dietetic therapy and is not comfortable with other therapies who call the patients to control and maintain a certain lifestyle. They have little experience in applying the principles of behavior change and have little opportunities to monitor their patients (who are undergoing a behavioral therapy) long enough to develop confidence in such a therapy.

Furthermore physicians are not comfortable with behavioral change therapy because success here is marked by small increments and recidivism and failure is common. They feel more comfortable when dealing with absolute terms like: health versus disease, normal versus abnormal, compliance versus non-compliance. This impulsivity and impatience to restore abnormal to normal is rewarded in the competitive pre-med environment and is implemented in the most part of the medical training and residency.

The fact that most of the successful programs like: weight management, stop smoking program, alcohol abstinence (Alcoholics Anonyms) are outside the classical health institutions and rarely use physicians as health vectors tells volumes about the inefficiency of physicians to implement behavioral change.

Lifestyle involves a multitude of variables which make it difficult to come up with a quick and simple message for the public. However, the scientific world need to find consensus about what message it delivers to the world. Harlan and Stross observed that a

critical issue in the above equation is education, education for both population and for medical professionals.
Harlan and Stross proposed in their article that focus of the educational effort for the prevention of CHD should be re-directed first and foremost on…physicians. They suggest that the whole medical training of future students should be designed differently than it is now in order to have physicians deal successfully with the challenges posed by the present epidemics of lifestyle diseases.

Change in the medical training is on the air but how soon?

Dr. Molly Cooke and al. complain in the New England Journal of Medicine that "Students learn from this culture that health care as a business may threaten medicine as a calling." Physicians are now paid for what they write on the chart, not for what they do for the patient. Physicians seem to be increasingly focused on treatment instead of prevention. In an average 15 minute visit patients explaining their problem to a physician were interrupted after an average of 23 seconds. Fifty percent of patients leave office visits not understanding what the physician has told them. It would take a primary care physician 18 hours per day to provide all recommended preventive and chronic care services to a typical patient panel. As a result, only half of evidence-based care is actually provided. These disturbing findings can be attributed primarily to the overburdened 15-minute clinician visit. The solution described by Dr. Bodenhaimer is chaning primary care into a team-based endeavor, offloading many functions from the 15-minute visit. This is exactly what we do now for 13 years at Herghelia Lifestyle Center.

"The future physician—regardless of specialty field—will need to manage an avalanche of patient-specific data, rapidly changing and ever-progressing scientific information, and new and evolving technology to support both diagnosis and treatment. Key Point: the physician of the future will need to combine high-tech medicine with high-touch caring…. Among those important skills will be the ability to establish trusting relationships with patients, for without trust effective care is impossible. The physician of the future will also have to recognize that professional obligations extend beyond the patients who come to the office or hospital. It will be necessary to take responsibility for the health of the public in their region and begin to become stewards of limited societal resources that must be applied in the most effective ways".
.
In conclusion: is it possible to extend these results to the general population translating them into recommendations and guides? Well is not only possible but according with the new thinking about reforming medical education it will be mandatory for future physicians to have also Public Health and Prevention vision while practicing patient care. Interventions in the area of behavior and lifestyle change are inevitably involved in the battle with all chronic disease and particularly with CHD. Essentially we are talking about an educational process in which patients understand physiology and its laws and are helped to learn behavior and techniques which are helping them to embrace a lifestyle dictated by the law of physiology and not by the whim of bed habits. The involvement of the physician in healthy behavior promotion is a must because it has a much bigger impact in patients than the involvement of nurses, auxiliary personnel and lay people.

Although the studies evaluating the impact of lifestyle upon the natural history of the CHD are hard to do because technical details like: difficult randomization, weak control, ethical issues, the difficulty to design simple or double blind studies, long term non-compliance, etc; although we cannot completely extrapolate all the results of these study to the general population, these studies are useful suggesting future direction for research, and a promise of a

new and better era for Public Health Education and Health Promotion. Hopefully there will be a day when these Cinderellas will be recognized for their true important role in the Medical Care.

REFERENCES

1. Smith S.C. et al., 1995, Preventing heart attack and death in patients with coronary disease. Circulation, Jul 1; 92(1):2-4
2. Hill JO, Wyatt HR, Phelan S, Wing RR., 2005, The National Weight Control Registry: is it useful in helping deal with our obesity epidemic? Journal of Nutrition Education and Behavior, 37: 206-210
3. Pekka P, 2002, Successful prevention of non-communicable diseases: 25 year experiences with North Karelia Project in Finland, Public Health Medicine, 4 (1):5-7
4. Vartiainen E, Puska P, Pekkanen J. d al., 1994, Changes in risk factor explains changes in mortality from ischemic heart disease in Finland. BMJ 309: 23-27.
5. Sanstrom P.H., 2002, Comunicare personală la Herghelia Euro-regional Conference on Quit and Win, 2002 for Health Professionals, March 15-17, 2002 Herghelia, Romania
6. Harlan W.R., Stross J.K., 1985, An educational view of a national initiative to lower plasma lipid levels. JAMA. 1985 Apr 12; 253(14):2087-90
7. Hjermann I. et al., 1981, Effect of diet and smoking intervention on the incidence of CHD: Report from the Oslo Study Group of a randomized trial in healthy men. Lancet 1981; 2: 1303-1310
8. Cooke M., Irby M.I., William S., Ludmerer K.M., 2006, American Medical Education 100 Years after the Flexner Report September 28, 2006, number 13, volume 355:1339-1344
9. Bodenheimer T. 2007, A 63-year-old man with multiple cardio-vascular risk factors and poor adherence to treatment plans. JAMA 2007;298:2048-2055.
10. Bodenheimer T., 2008, Transforming Practice. The future of primary care. N Engl J Med, November 13, 2008, Number 20, Volume 359:2086-2089
11. Bodenheimer T., 2008, Transforming Practice. The future of primary care. N Engl J Med, November 13, 2008, Number 20, Volume 359:2086-2089
12. Smith G. L., 2008, The future of medical training: Back to basics in a new world, The Journal of Family Practice: : Current Clinical Practice October 2008 · Vol. 57, No. 10A Suppl: S14-S16.
13. Kottke T.E., Solberg L.I., Brekke M.L., Conn S.A., Maxwell P., Brekke M.J., 1992, A controlled trial to integrate smoking cessation advice into primary care practice: Doctors Helping Smokers, Round III. J Fam Pract. 1992 Jun; 34(6):701-8

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