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Effectiveness of motivational counseling for lifestyle modification in obese patients using a patient-centered approach

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Obesity is a predictor of a significant number of non-communicable diseases. Reduction of body weight by 5–10 % in 6 months, has a positive effect on the prognosis of life and is one of the goals of treatment. To achieve such goals, there is a need for a patient-oriented approach, where the degree of individualization corresponds to the personal risks and needs of the patient with his involvement in the process of choosing a treatment strategy and forming new flexible life habits through the use of motivational counseling.
The objective: **is to determine the effectiveness of motivational counseling for lifestyle modification in obese patients of prime working age using a patient-oriented approach.**
Materials and methods**. 37 patients with obesity I (27 people) and II (10 people) degree, aged 38.03±1.27 years (20 women and 17 men) were examined. Patients were given motivational counseling according to the «5 A's» system, the patient-oriented approach included recommendations regarding the regime and caloric content of food, physical activity (monitoring with a pedometer), compliance with sleep hygiene, correction of psycho-emotional disorders.**
Clinical laboratory examination in dynamics after 1 month, 3 months and 6 months included measurements of BMI, waist and hip circumference, body surface area, waist/hip ratio, conicity index, body shape index, abdominal volume index, blood pressure, levels of blood glucose, insulin, HOMA index, cholesterol, lipidogram indicators, serotonin and leptin.
In addition, surveys were conducted using the HADS hospital anxiety and depression scale, Beck's scale, Hamilton scale, Dutch Eating Behavior Questionnaire, Epworth Sleepiness Scale, Pittsburgh Sleep Quality Questionnaire, SF-36, The International Physical Activity Questionnaire, The Finnish Diabetes Risk Score. Statistical analysis was performed using IBM SPSS Statistics, Statistica 12, descriptive statistics Excel 2010.
Results**. During 6 months of observation, patients lost more than 5 % of their body weight ($p<0.05$), which was accompanied by a significant decrease in BMI ($p<0.01$) and an increase in the level of physical activity ($p<0.001$). The levels of lipid and carbohydrate metabolism exceeded the recommended values and had a positive tendency to decrease during treatment ($p>0.05$). Assessments of the manifestations of anxiety and depression according to the HADS depression and Hamilton scales, eating disorders, serotonin and leptin levels, quality of sleep, quality of life of patients improved. The prediction of the risk of developing diabetes had significant positive dynamics ($p<0.05$).**
Conclusions**. The obtained results make prove that the application of of motivational counseling according to the step-by-step system «5 As» with a patient-oriented approach in patients of working age with obesity is an effective method, which is confirmed by reliable positive results and allows to reduce body weight by more than 5 % in 6 months, reduce levels of metabolic disorders, blood pressure, increase physical activity, reduce the manifestations of depression and anxiety, eating disorders, improve the quality of sleep and life of patients, improve the prognosis and reduce the risk of non-infectious diseases. If it is necessary to achieve stricter targets of indicators in obese patients and/or in a shorter time, it is necessary to carry out a further search for effective measures and consider the additional use of pharmaceutical products in prevention.**
Keywords: *motivational counseling, patient-centered care, obesity, anxiety, depression, sleep disorders, eating behavior, serotonin, leptin, lifestyle modification.*

Ефективність мотиваційного консультування щодо корекції способу життя у пацієнтів з ожирінням з використанням пацієнт-орієнтованого підходу

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Ожиріння є предиктором значної кількості неінфекційних захворювань. Зниження маси тіла на 5–10 % за 6 міс має позитивний вплив на прогноз життя і є однією з цілей лікування. Для досягнення таких цілей виникає потреба пацієнт-орієнтованого підходу, де ступінь індивідуалізації відповідає персональним ризикам та потребам пацієнта з його залученням до процесу обрання стратегії лікування та формуванням нових гнучких життєвих звичок шляхом використання мотиваційного консультування.
Мета дослідження: визначення ефективності застосування мотиваційного консультування щодо корекції способу життя у пацієнтів основного працездатного віку з ожирінням з використанням пацієнт-орієнтованого підходу.
Матеріали та методи. Обстежено 37 пацієнтів з ожирінням I (27 осіб) та II (10 осіб) ступеня, віком 38,03±1,27 року (20 жінок та 17 чоловіків). Пацієнтам проводили мотиваційне консультування за системою «5 As». Пацієнт-орієнтований підхід включав рекомендації щодо режиму і калорійності харчування, фізичної активності (контроль за допомогою крокоміра), дотримання гігієни сну, корекції психоемоційних розладів.

Клініко-лабораторне обстеження в динаміці через 1 міс, 3 міс та 6 міс включало вимірювання ІМТ, об'єму талії та стегон, площі поверхні тіла, співвідношення талії/стагон, індексу конусності, індексу форми тіла, індексу абдомінального об'єму, артеріального тиску, рівнів у крові глюкози, інсуліну, індексу HOMA, холестерину, показників ліпідограми, серотоніну та лептину.

Додатково проводили опитування за допомогою госпітальної шкали тривоги та депресії HADS, шкали Бека, шкали Гамільтона, Голландського опитувальника харчової поведінки, Epworth Sleepiness Scale, Пітсбурзького опитувальника якості сну, SF-36, The International Physical Activity Questionnaire, The Finnish Diabetes Risk Score. Статистичний аналіз здійснювався за допомогою IBM SPSS Statitics, Statistica 12, описова статистика Excel 2010.

Результати. За 6 міс спостереження пацієнти втратили більш ніж 5 % маси тіла ($p<0,05$), що супроводжувалось достовірним зменшенням ІМТ ($p<0,01$) та підвищенням рівня фізичної активності ($p<0,001$). Рівні ліпідного та вуглеводного обмінів перевищували рекомендовані значення та мали позитивні тенденції до зниження у процесі лікування ($p>0,05$). Покращилися рівні тривоги і депресії за шкалами $HADS_{депресія}$ та Гамільтона, порушення харчової поведінки, рівні серотоніну та лептину, якість сну, якість життя пацієнтів. Прогноз ризику виникнення цукрового діабету мав суттєву позитивну динаміку ($p<0,05$).

Висновки. Застосування методики мотиваційного консультування за системою «5 A^s» з пацієнт-орієнтованим підходом у пацієнтів з ожирінням є ефективною методикою, що підтверджується достовірними позитивними результатами та дозволяє знизити масу тіла на більш ніж 5% за 6 міс, знизити рівні метаболічних порушень, артеріального тиску, підвищити фізичну активність, зменшити прояви депресії та тривоги, порушення харчової поведінки, покращити якість сну та життя пацієнтів, покращити прогноз та знизити ризик виникнення неінфекційних захворювань.

У разі необхідності досягнення у пацієнтів з ожирінням більш жорстких цільових показників та в коротші терміни необхідно здійснювати подальший пошук ефективних заходів та розглядати додаткове застосування медикаментозних засобів профілактики.

Ключові слова: *мотиваційне консультування, пацієнт-орієнтована допомога, ожиріння, тривожність, депресія, розлади сну, харчова поведінка, серотонін, лептин, модифікація способу життя.*

Obesity in the world is rapidly developing every year, and is a predictor of a significant number of non-infectious diseases [1–9]. An increase in BMI by five units above 25 kg/m^2 contributes to an increase in total mortality by 29%, from vascular diseases by 41 % and mortality associated with diabetes by 210% [10].

A decrease in body weight has a positive effect on the prognosis of life – with a weight loss of 5–10 % in 6 months, the risk of developing diabetes and other non-infectious diseases decreases by 44 % [11–14]. A significant number of associations such as the World Health Organization (WHO), World Obesity Federation (WFO), Obesity Canada, Obesity Medicine Association (OMA), Obesity Action Coalition (OAC), European Association for the Study of Obesity (EASO), Obesity Policy Engagement Network (OPEN), European Society for Clinical Nutrition and Metabolism (ESPEN), The Obesity Society (TOS), American Society For Metabolic And Bariatric Surgery (ASMBS) consider and offer the latest methods of obesity treatment, however, the "basic" therapy is based on modification lifestyle, in most recommendations, a single method is used: reducing energy consumption and increasing its expenditure ("eat less, move more") [11, 14–16].

Reducing energy consumption by 500–1000 kcal per day helps to reduce body weight by 0.5–1 kg per week, eliminating hypodynamism in patients with the provision of a minimum physical load of 10,000 steps per day also helps to improve the patient's prognosis [14, 17]. To achieve such goals, there is a need for teamwork with a patient-oriented approach, where the degree of individualization corresponds to the personal risks and needs of the patient with his involvement in the process of choosing a treatment strategy and the formation of new flexible life habits through the use of motivational counseling [11, 14, 18–21].

For a long time, psychotherapeutic methods have been introduced and improved in medicine, which help the patient to change destructive behavioral habits, including the BATHE technique, FRAMES, the 5As model, the Stages of Change (Transtheoretical model). The BATHE technique is a short psychotherapeutic method that addresses the patient's most troubling problem with an emphasis on encouraging independent resolution [22].

In 1983, V. Miller and S. Rollik developed the concept of motivational counseling based on the experience of treating alcoholism, which was defined as a client-centered approach in counseling, aimed at preparing the client for changes by identifying and overcoming his ambivalence and strengthening motivation, a person's commitment to change [23]. Also known are the methods of motivational interviewing using step-by-step guidelines for change FRAMES (Feedback, Responsibility, Advice, Menu Options, Empathy, and Self-Efficacy) [24] and the Stages of Change (Transtheoretical Model) developed by Prochaska and DiClemente in the late 1970s x years, which developed thanks to research on the experience of smokers (Precontemplation, Contemplation, Preparation (Determination), Action, Maintenance, Termination [25, 26].

The "5 As" system was also created as a method of changing the behavior of people who smoke [27], it is a model for use by primary care physicians to promote patient behavior change and best adapt for obese patients [28]. The Canadian obesity network, Obesity Canada, has developed a clinical practice guideline that includes an approach to obesity management in primary care settings. assistance using the "5 As" system, which allows you to divide the treatment process into stages. It includes 5 steps: 1 – "Ask" – where the doctor should ask permission to discuss weight and explore the patient's readiness for change, recognize that obesity is a chronic disease; 2 – "Assess" - carrying out an assessment of the risks associated with obesity, the "main causes" of obesity and obstacles that interfere with treatment; 3 – "Advise" providing advice on reducing health risks and treatment options; 4 – "Agree" – agreement on health outcomes

and behavioral goals; 5 – "Assist" – help to find available appropriate resources to ensure the goal [11], all stages must be worked out at each patient visit.

For working patients, it is quite important to take into account their life characteristics in the treatment process, because without existing complications, this group of patients rarely seeks help on their own, which should be taken into account by primary care doctors. In addition, the effectiveness of a patient-oriented approach during motivational counseling, which would take into account the specifics of the work schedule, sleep disorders, psycho-emotional state during motivational counseling of obese patients regarding lifestyle modification, remains poorly studied.

The objective: is to determine the effectiveness of motivational counseling for lifestyle modification in obese patients of prime working age using a patient-oriented approach.

MATERIALS AND METHODS

37 patients with obesity I (27 people) and II (10 people) degree, aged 38.03±1.27 years (20 women and 17 men) were examined. In order to manage obesity, all patients were given motivational counseling on lifestyle modification according to the 5 As system, where goals of weight loss of 5–10% in 6 months were set with the caloric content of the daily ration according to the WHO formula for calculating energy costs [11]. The patient-oriented approach included recommendations regarding the regime and caloric content of food, physical activity (monitoring with a pedometer), compliance with sleep hygiene, and correction of psycho-emotional disorders.

With purpose to evaluate the effectiveness of the applied aproach, the monitoring of patients was provided at the beginning of the study and in dynamics after 1 month, 3 months, and 6 months with measurement of Body Mass Index (BMI), Waist Circumference (WtC) and Hip Circumference (HC), and other anthropometric indicators were calculated, such as Body Surface Area (BSA), Waist-to-Hip Ratio (WHR), Conicity Index (ConI), a Body Shape Index (ABSI), Abdominal Volume Index (AVI).

Clinical laboratory examination included measurements of blood pressure (BP), blood levels of glucose, insulin, HOMA index, cholesterol, lipidogram indicators, serotonin and leptin. Psychosocial status was assessed using the Hospital Anxiety and Depression Scale (HADS), the Beck Scale, the Hamilton Scale (HAM-A), the Dutch Eating Behavior Questionnaire (DEBQ), the Epworth Sleepiness Scale (ESS), the Pittsburgh Sleep Quality Questionnaire (PSQI), quality of life – SF-36, the International Physical Activity Questionnaire (IPAQ), the Finnish Diabetes Risk Score (FINDRISC). Statistical analysis was performed using IBM SPSS Statistics, Statistica 12, descriptive statistics Excel 2010.

THE RESULTS AND DISCUSSION

At the beginning of the study (Table), body weight was 94.44±2.33 kg, there was no significant difference between women and men ($p>0.05$). BMI was 33.47±0.50 kg/m^2 (33.88±0.53 in women and 33.00±0.46 in men, $p>0.05$), which corresponded to I and II degrees of obesity. Waist circumference (WtC) was 1.04±0.02 m, there was no statistical difference between women (1.01±0.01 m) and men (1.06±0.02 m). Wt indicators exceeded the WHO recommended values for men (>94 cm) and women (>80 cm) in Europe, which indicates an increase in cardiovascular risks in patients [29, 30]. A similar trend was observed with defined hip circumference (HC).

Abdominal type of obesity was confirmed by WHR, BSA, ConI, ABSI and AVI indices (Table). When analyzing them in terms of gender, no significant difference was found between men and women according to ConI ($p_0=0.15$; $p>0.05$), ABSI ($p_0=0.08$; $p>0.05$) and AVI ($p_0=0.17$; $p>0.05$), it was present when determining BSA ($p_{1\text{-}6\ months}=0.03$; $p<0.05$) and WHR ($p_0=0.04$; $p<0.05$). Obesity is a predictor of the development of many non-infectious diseases and often contributes to the development of arterial hypertension, impaired carbohydrate and lipid metabolism, hypodynamia, etc.

The results of the clinical and laboratory examination of the patients revealed normal high blood pressure levels, both systolic (BPs=135.54±2.36 mmHg) and diastolic (BPd=86.76±1.78 mmHg), which also did not depend on gender. Violations of carbohydrate tolerance and insulin resistance were determined in the patients (Table). The risk of diabetes (FINDRISC=14.16±0.61) was moderate, and according to the forecast for the next 10 years, it could occur in every 6th patient. Disorders of lipid metabolism were characterized by exceeding target levels [53] of total cholesterol and LDL, HDL levels were below 1.2 mmol/l in only 5 patients, with an average of 1.55±0.05 mmol/l, which corresponded to their normal values. VLDL corresponded to the reference (M±m0=0.82±0.05). The atherogenicity index also did not go beyond the permissible values (2.86±0.20).

Physical activity of patients (IPAQ) at the initial level was on the border of hypodynamia (21.08±1.76), which is quite important in this group of patients, and there was no significant difference between genders ($p=0.66$; $p>0.05$).

When examining the mental health of patients (Table), it was determined the presence of subclinical depression on the HADS depression scale (10.19±0.75 points) and on the Beck scale (10.70±0.95 points) – a mild degree of depression (subdepression). The presence of anxiety in patients was confirmed by the average score on the HADS anxiety scale (8.59±0.61 points) and on the Hamilton scale (9.70±0.53 points), which corresponds to clinically expressed anxiety. These indicators had no gender differences.

The eating behavior of patients according to the Dutch Eating Behavior Questionnaire (DEBQ) was disturbed, namely, according to the scale of the Emotional eating, a tendency to "eat emotions" was noted (M±m = 2.82±0.34 points); according to the scale of the External eating, the tendency of patients to overeat was revealed when food was available at the initial level of 3.38±0.15 points; according to the Restrained eating scale, the habit of eating without restrictions was also noted at 3.87±0.12 points.

When studying sleep disorders and sleepiness using Epworth and PSQI Global score questionnaires, it was determined that patients had moderate daytime sleepiness

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(Epworth = 7.41±0.59 points) and low sleep quality (PSQI Global score = 7.54±0,46 points). After considering all the components of the questionnaire, it was noted that Sleep quality was 1.89±0.15, which indicated the characteristics of sleep by the patients themselves as poor quality sleep (0.97±0.09). Sleep latency at the first stage was 1.54±0.14 points, which meant the inability of patients to fall asleep within 30–60 minutes, 1–2 times a week on average in the group. Sleep duration at the initial level was 0.92±0.17 points, which indicates the sleep duration estimated by the patients at 6 hours per night. Habitual sleep efficiency was estimated at 0.35±0.08 points. Sleep disturbance was 1.49±0.08, which indicates episodes of waking up at night, difficulty breathing, snoring, feeling pain, cold, heat, bad dreams 1–2 times a night.

Use of sleeping medication, showed that only 1 patient had episodes of using sleeping medications. Daytime dysfunction was 1.32±0.10 points, which indicated the difficulty for patients 1–2 times a week to maintain a sufficient mood to be socially active and perform their tasks. The quality of life of patients according to the SF36 questionnaire for all components (Physical Functioning – PF, Bodily Pain – BP, General Health – GH, Social Functioning – SF, Vitality – VT, Mental Health – MH, (Role Emotional – RE) was below average at the beginning research.

The close pathogenetic connection between the level of mental and metabolic disorders in patients was accompanied by changes in the hormonal background. It has been proven that the development of anxiety and depression is accompanied by a decrease in serotonin concentration [31, 32], so overeating in obese patients is the main mechanism for supplying the body with serotonin and dopamine [33, 34].

Serotonin affects not only the mood, but also the regulation of the circadian rhythm and food consumption through a direct effect on adipose tissue [32, 33, 35–42]. It is formed in the central nervous system in the brain stem and hypothalamus and the pineal gland, and its synthesis is carried out in the periphery in the enenterochromatophilic cells of the gastrointestinal tract [32, 33, 36, 43–45].

The action of serotonin has been confirmed experimentally, with the peripheral administration of a tryptophan-hydroxylase inhibitor, its metabolism decreases and its concentration in the blood and across the blood-brain barrier increases, and as a result, a decrease in body weight is observed even in individuals with hyperphagia and obesity [46]. Leptin is a peripheral hormone secreted by adipocytes and affects the hypothalamus and limbic system, which control emotions, motivation, behavior, according to the principle of feedback, reduces appetite and promotes weight loss [47–51].

The level of serotonin in the blood of the patients in our study at the first visit had a low reference value of 155.46±3.07 μg/L, which indicates its low levels (Table). The level of leptin exceeded normal values, which confirms the presence of hormonally active adipose tissue in patients with abdominal obesity. It is advisable to consider it for each gender separately, in connection with different reference values (female = 3.7–11.1 ng/ml; male = 2.0–5.6 ng/ml). The average level of leptin in women (11.13±1.25 ng/ml) and men (9.90±0.98 ng/ml) exceeded normal values.

The obtained data indicate the presence of a complex of psycho-social, behavioral and clinical-laboratory disorders in obese patients, which requires a comprehensive patient-oriented approach during the application of the motivational counseling method according to the «5 As» system with the establishment of a target weight loss within 5–10% in 6 months.

The first point of control of the effectiveness of the technique was carried out after 1 month. As can be seen from Table, the percentage of body weight loss during this period was reliably significant ($p<0.05$), however, BMI did not have a significant difference. Waist circumference (WtC) moderately decreased to 1.01±0.02 m, ($p>0.05$), although it also exceeded the recommended values [30]. Abdominal obesity indices WHR, BSA, ConI, ABSI and AVI did not change significantly.

Arterial pressure, both systolic and diastolic (BPd=86.76±1.78 mm Hg) did not undergo significant changes pBPs=0.53/pBPd=0.27 ($p>0.05$); the same dynamics were observed for indicators of lipid metabolism, carbohydrate metabolism and leptin, both in men and in women ($p>0.05$). The prognosis of developing diabetes in the next 10 years (FINDRISC) remained the same ($p=0.45$). The level of physical activity (IPAQ) increased, although not significantly ($p=0.33$; $p>0.05$), but already had normal values (23.30±1.40). However, the level of serotonin in the patients' blood increased unreliably to 160.03±3.50 μg/l ($p=0.34$; $p>0.05$).

The degree of depression according to the HADS depression scale significantly decreased (7.70±0.63 points, $p=0.01$) and corresponded to the subclinical degree, however, according to the Beck scale, it increased significantly (13.84±1.12 points, p=0,04), but remained within the assessment range corresponding to a mild degree of depression (subdepression). The level of anxiety after 1 month reliably increased on the $HADS_{anxiety}$ scale (10.49±0.47 points; $p=0.02$), but on the Hamilton scale it decreased, but not reliably (9.41±0.54 points; $p=0.70$). Changes in eating behavior in patients (DEBQ) after 1 month were reflected in an increase in scores on the scale of the Emotional eating, the tendency to "eat emotions" increased ($p=0.68$; $p>0.05$).

According to the scales of External and Restrained eating, the tendency to overeat significantly decreased ($p=6.12E-03$ and $p=0.01$, respectively), although it did not reach the target values. Moderate daytime sleepiness (Epworth =8.70±0.67 points; $p>0.05$) remained at this stage, but the quality of sleep PSQI Global score significantly improved (6.08±0.27 points; $p=0.009$). Most of the components of the PSQI questionnaire during the first month of observation had reliably positive changes (Sleep quality, Sleep latency, Sleep duration, Sleep disturbance, Daytime dysfunction – $p<0.05$), with the exception of Habitual sleep efficiency and Use of sleeping medication ($p>0,05$).

Dynamic observation of the quality of life of patients according to the SF36 questionnaire after 1 month of using motivational counseling revealed a statistically significant improvement in the quality of life according to Physical Functioning – PF, Vitality – VT ($p<0.05$), other changes in the components of the quality of life were not

so expressed (Bodily Pain – BP, General Health – GH, Social Functioning – SF, Mental Health – MH, Role Emotional – RE – p>0.05).

After 3 months (Table), when assessing the effectiveness of motivational patient-oriented counseling according to the «5AS» system, more and more positive effects were noted, in contrast to the initial level and the results after 1 month, in particular, the percentage of body weight loss significantly increased to 2.99±0.19% (p<0.001), but BMI, WtC and indicators of abdominal obesity did not change significantly. Blood pressure levels have significantly decreased: BPs to 130.00±1.44 mm Hg. Art. (p=0.05), BPd to 81.49±0.87 mm Hg. Art. (p=1.08E-02). Indicators of carbon and lipid metabolism were at the same level as a month later.

The 10-year prediction of the development of diabetes (FINDRISC) remained the same, although the decrease in scores was reliable (12.32±0.56; p=0.03; p<0.05), but not sufficient. The physical activity of patients significantly increased to 26.08±1.53 points (p=0.04; p<0.05). Indicators of depression according to the HADS depression scale (6.92±0.53 points) almost normalized with a significant change (p=7.63E-04), there was also a moderate and significant decrease in anxiety according to the Hamilton scale to 8.35±0.38 points (p = 0.04), but the level of depression according to the Beck scale and anxiety according to the HADS anxiety scale did not change significantly. Changes in eating behavior also changed, although they did not reach the recommended values.

The level of sleep quality (PSQI), the patients' quality of life according to the SF36 questionnaire, had the same trends as after the first month of observation. The level of serotonin increased insignificantly to 163.68±3.80 μg/ml (p=0.10; p>0.05). Average leptin levels had a tendency to decrease without significant significance (p = 0.51; p > 0.05), however, in women there was a normalization of indicators to 10.23±1.31 ng/ml (p_{3month}=0.72; p>0.05), and in men leptin fluctuations did not reach reference values (p_{3month}=0.53; p>0.05).

After 6 months of using motivational patient-oriented counseling (Table) the body weight loss goals were achieved by more than 5%, which was reliably significant (p < 0.05). BMI significantly decreased to 31.62±0.46 kg/m^2 (p=0.009; p>0.05). WtC decreased to 0.99±0.02 m, but not reliably (p=0.09; p>0.05), and exceeded the recommended values [29], the same situation was with the indicators of abdominal obesity.

Blood pressure levels at the end of the study stabilized and reached normal values (128.24±1.69)/(80.54±0.91) mm Hg. Art. (pBPs=1.56E-02/pBPd=3.12E-03; p<0.05). Physical activity indicators (IPAQ) were significantly normalized to 30.16±1.64 points (p=3.83E-04; p<0.001). The levels of glucose and the index of insulin resistance tended to decrease and normalize, but without significant changes, so the manifestations of impaired carbohydrate tolerance and insulin resistance remained, although the level of insulin decreased significantly, reaching a level of 14.54±0.95 μIU/ml (p=4.58E-02; p<0.45) compared to the initial level and the prognosis of the occurrence of diabetes in the next 10 years improved (up to 11.14±0.55 points, p=5.04E-04; p<0.001), the risk of developing diabetes in the next 10 years was 1 in 25 patients, which confirms the effectiveness of motivational counseling based on the "5As" system in obese patients.

Total cholesterol and LDL cholesterol tended to decrease, but did not reach the target levels, LDL cholesterol significantly decreased (p=4.91E-02) and corresponded to reference values (0.70±0.04). HDL concentration significantly increased to 1.69±0.27 mmol/l, (p=3.90E-02). The atherogenicity index did not undergo statistically significant changes and also did not go beyond the permissible values (2.40±0.22; p=0.13). The obtained data indicate the insufficient effect of only lifestyle modification and indicate the need to use additional methods of drug prevention.

Mean leptin levels gradually decreased to the range of reference values in women (9.43±1.28 ng/ml), although there was no significant difference in both women (p=0.50) and men (p=0.33), however, unlike women, normalization of indicators was not observed in men (7.84±0.94 ng/ml). The level of serotonin in the patients' blood, when compared with the initial level, after 6 months increased to 166.35±3.57 μg/l, which was reliably significant (p=2.56E-02; p<0.05).

Depression by the HADS scale (Table) significantly decreased in 6 months and was absent in patients and corresponded to normal values of 5.30±0.46 (p=5.47E-07; p>0.05). However, until the end of the 6th month, the indicators on the Beck scale did not change significantly and tended to slightly deviate (up to 12.11±1.13), which may be related to restrictions or discomfort regarding changes in lifestyle and nutrition. The level of anxiety significantly decreased to 7.54±0.30 (HAMA-A; p<0.05) and 8.24±0.41 ($HADS_{anxiety}$; p>0.05), approaching normal values.

Changes in eating behavior in patients, according to the DEBQ, on the scale of Emotional eating the tendency to "eat emotions" by the end of 6 months of the study, statistically decreased (p<0.05), although they did not reach normal values. According to the scale of the External eating, the normalization of indicators at the end of the study (2.32±0.16 points) and the disappearance of the tendency to overeat when food was available were found, which was reliable in comparison with the initial level (p=1.07E-05; p<0.001).

The Restrained eating scale also demonstrated the positive effects of motivational counseling on the patients' eating behavior – they were better able to limit themselves in consuming excessive amounts of food, which was confirmed by the normalization of the scale indicators 2.75±0.14 (p=5.02E-08; p<0.001) and proves the effectiveness of motivational patient-oriented counseling of obese patients of prime working age in Ukraine. Epworth moderate daytime sleepiness (ESS) tended to decrease without a significant difference (6.73±0.50 points, p>0.05), indicating insufficient means of correcting this condition.

Sleep quality (PSQI Global score) improved significantly with a significant difference and normalization (3.76±0.20; p=1.99E-10; p<0.001), Sleep quality reached the level of 0.97±0.09 (p=2.25E-06; p<0.001) and was defined as sleep of sufficiently good quality. Sleep latency significantly changed (0.70±0.10; p=9.00E-06; p<0.001),

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Dynamics of patient indicators, M±m

Indicator		Baseline, n=37	1 month, n=37	3 month, n=37	6 month, n=37
Weight, kg		94.44±2,33	92.75±2,27	91.61±2,26	89.13±2.08
% of body weight loss		1.77±0.17$^{***\#\#\#}$		2.99±0.19$^{***\#\#\#}$	5.51±0.2$^{***\#\#\#}$
BMI, kg/m^2		33.47±0.50	32.88±0.49	32.47±0.48	31.62±0.46$^{\#\#}$
WtC, m		1.04±0,02	1.01±0.02	1.01±0,02	0.99±0.02
HC, m		1.16±0,02	1.14±0.02	1.14±0.02	1.12±0.02
BSA, м^2		2.13±0.03	2.12±0.03	2.10±0.03	2.08±0.03
WHR		0.90±0.01	0.89±0.01	0.89±0.01	0.88±0.01
ConI, м$^{3/2}$/кг$^{1/2}$		1.27±0.02	1.25±0.02	1.25±0.02	1.25±0.02
ABSI, м$^{5/3}$·кг$^{-2/3}$		0.0770±0.0009	0.0763±0.0009	0.0765±0.0009	0.0765±0.0009
AVI		21.89±0.82	21.02±0.81	20.78±0.79	20.03±0.75
BPs, mmHg		135.54±2.36	133.65±1.81	130.00±1.44	128.24±1.69$^{\#\#}$
BPd, mmHg		86.76±1.78	84.46±0.99	81.49±0.87*	80.54±0.91$^{\#\#}$
Glucose, mmol/l		6.29±0.16	6.58±0.15	6.31±0.15	6.08±0.15
Insulin, μIU/ml		17.02±0.75	15.82±0.92	15.13±0.84	14.54±0.95$^{\#}$
HOMA index, μmol·μl·ml^2		4.87±0.29	4.78±0.34	4.37±0.31	4.06±0.33
Total cholesterol, mmol/l		5.64±0.16	5.46±0.19	5.37±0.21	5.42±0.24
HDL, mmol/l		1.55±0.05	1.63±0.05	1.58±0.05	1.69±0.04$^{\#}$
LDL, mmol/l		3.88±0.15	3.90±0.17	3.85±0.15	3.50±0.19
VLDL, mmol/l		0.82±0.05	0.73±0.05	0.81±0.04	0.70±0.04$^{*\#}$
Atherogenic index		2.86±0.20	2.55±0.20	2.61±0.22	2.40±0.22
Serotonin, μg/l		155.46±3.07	160.03±3.50	163.68±3.80	166.35±3.57$^{\#}$
Leptin, ng/ml		10.56±1.14	9.88±1.16	9.48±1.17	8.70±1.15
Hamilton anxiety scale, points		9.70±0.53	9.41±0.54	8.35±0.38$^{\#}$	7.54±0.30$^{\#\#\#}$
HADS, points	anxiety	8.59±0.61	10.49±0.47$^{*\#}$	9.51±0.44	8.24±0.31*
	depression	10.19±0.75	7.70±0,63$^{*\#}$	6.92±0,53$^{\#}$	5.30±0.46$^{*\#\#\#}$
Beck's (depression scale), points		10.70±0.95	13.84±1.12$^{*\#}$	12.78±0.79	12.11±1.13
DEBQ,points	Emotional eating	2.82±0,16	2.91±0.14	2.64±0.12	2.08±0.12$^{**\#\#\#}$
	External eating	3.38±0.15	2.76±0.16$^{**\#\#}$	2.56±0.16$^{\#\#\#}$	2.32±0.16$^{\#\#\#}$
	Restrained eating	3.87±0.12	3.42±0.13$^{*\#}$	3.13±0.13$^{\#\#\#}$	2.75±0.14$^{*\#\#\#}$
PSQI Global score, points		7.54±0.46	6.08±0.27$^{**\#\#}$	4.76±0.24$^{***\#\#\#}$	3.76±0.20$^{**\#\#\#}$
Drowsiness (ESS), points		7.41±0,59	8.70±0.67	8.05±0.58	6.73±0.50
SF-36, points	PF	69.32±2.57	79.19±2.14$^{**\#\#}$	81.76±2.38$^{\#\#\#}$	88.11±2.08$^{\#\#\#}$
	RP	50.68±6.08	56.76±5.54	57.43±4.95	65.54±4.81
	BP	64.97±4.58	65.76±4.61	64.86±4.25	78.54±3.20$^{*\#}$
	GH	49.72±3.54	48.58±3.64	57.04±3.53	71.26±3.43$^{**\#\#\#}$
	VT	51.62±2.36	59.46±2.75$^{*\#}$	63.24±2.92$^{\#\#}$	71.62±2.77$^{*\#\#\#}$
	SF	55.41±4.07	58.78±3.97	62.84±3.19	72.64±3.47$^{*\#\#}$
	RE	45.93±6.78	52.23±5.77	52.74±5.38	68.43±4.41$^{*\#\#}$
	MH	51.78±4.14	55.46±3.81	61.62±3.29	71.78±3.13$^{*\#\#\#}$
IPAQ, points		21.08±1.76	23.30±1.40	26.08±1.53$^{\#}$	30.16±1.64$^{\#\#\#}$
FINDRISC		14.16±0,61	13.51±0,57	12.32±0.56$^{\#}$	11.14±0.55$^{\#\#\#}$

Note: * – p<0.05, ** – p<0.01, *** – p<0.001 – in comparison with the previous control point. $^{\#}$ – p<0.05, $^{\#\#}$ – p<0.01, $^{\#\#\#}$ – p<0.01 – in comparison with the initial values.

which indicates a decrease in the number of minutes of falling asleep (up to 15 minutes).

Sleep duration by the end of 6 months of observation stabilized significantly (p=8.41E-05; p<0.001) to 0.14±0.08 points, which is interpreted as an extension of sleep to more than 7 hours/night. Habitual sleep efficiency significantly improved to 0.08±0.04 points (p=4.30E-03; p<0.01), which also indicated the effectiveness of measures and improvement of sleep by more than 85%.

Sleep disturbance significantly changed to 1.05±0.04 (p=1.09E-05; p<0.001), which indicates a decrease in episodes of waking up at night, bad dreams, feeling pain, cold, heat, difficulty breathing, snoring from 1–2 times to less than once per night. Use of sleeping medication, showed that only 1 patient had episodes of using sleeping medications. Daytime dysfunction showed a significant decrease in scores to 0.78±0.09 points (p_{6month}=1.54E-04; p<0.001), which indicates the difficulty for patients 1–2 times a week to maintain a sufficient mood to be socially active and do their chores at the start of the study and improvement before its completion.

Dynamic observation of the quality of life of patients according to the SF36 questionnaire (Table) for 6 months with the use of motivational counseling revealed

a significant improvement in the quality of life in all components (Physical Functioning – PF, Bodily Pain – BP, General Health – GH, Social Functioning – SF, Vitality – VT, Mental Health – MH, (Role Emotional – RE), in addition to role functioning (pRP=0.06; p>0.05), which is included in the description of the state of the physical component of health (PF, RP, BP, GH) and indicates a low level of physical condition of patients and difficulties in everyday life and work (expenditure of additional efforts, time, limitations in the performance of some types of work, performance of smaller volumes than the patient wanted).

The obtained results indicate the achievement of the quality level life above the average for 6 months according to the indicators of the physical and mental components of the SF36 questionnaire.

CONCLUSIONS

The obtained results make prove that the application of of motivational counseling according to the step-by-step system "5 As" with a patient-oriented approach in patients of working age with obesity is an effective method, which is confirmed by reliable positive results and allows to reduce body weight by more than 5% in 6 months, reduce levels of metabolic disorders, blood pressure, increase physical activity, reduce the manifestations of depression and anxiety, eating disorders, improve the quality of sleep and life of patients, improve the prognosis and reduce the risk of non-infectious diseases.

If it is necessary to achieve stricter targets of indicators in obese patients and/or in a shorter time, it is necessary to carry out a further search for effective measures and consider the additional use of pharmaceutical products in prevention.

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REFERENCES

1. Bray GA, Kim KK, Wilding JPH; World Obesity Federation. Obesity: a chronic relapsing progressive disease process. A position statement of the World Obesity Federation. Obes Rev. 2017;18(7):715-23. doi: 10.1111/obr.12551.
2. Bray GA, Heisel WE, Afshin A, Jensen MD, Dietz WH, Long M, at al. The Science of Obesity Management: An Endocrine Society Scientific Statement. Endocr Rev. 2018;39(2):79-132. doi: 10.1210/er.2017-00253.
3. Afshin A, Forouzanfar MH, Reitsma MB, Sur P, Estep K, Lee A, et al. The GBD 2015 Obesity Collaborators. Health effects of overweight and obesity in 195 countries over 25 years. N Engl J Med. 2017;377:13-27. doi: 10.1056/NEJ Moa1614362.
4. Bjerregaard LG, Jensen BW, Ängquist L, Osler M, Sørensen TIA, Baker JL. Change in Overweight from Childhood to Early Adulthood and Risk of Type 2 Diabetes. N Engl J Med. 2018;378(14):1302-12. doi: 10.1056/NEJMoa1713231.
5. Hjort R, Ahlqvist E, Carlsson PO, Grill V, Groop L, Martinell M, et al. Overweight, obesity and the risk of LADA: results from a Swedish case-control study and the Norwegian HUNT Study. Diabetologia. 2018;61(6):1333-43. doi: 10.1007/s00125-018-4596-0.
6. Kyrgiou M, Kalliala I, Markozannes G, Gunter MJ, Paraskevaidis E, Gabra H, et al. Adiposity and cancer at major anatomical sites: umbrella review of the literature. BMJ. 2017;356:j477. doi: 10.1136/bmj.j477.
7. Koliaki C, Liatis S, Kokkinos A. Obesity and cardiovascular disease: revisiting an old relationship. Metabolism. 2019;92:98-107. doi: 10.1016/j.metabol.2018.10.011.
8. Anis AH, Zhang W, Bansback N, Guh DP, Amarsi Z, Birmingham CL. Obesity and overweight in Canada: an updated cost-of-illness study. Obes Rev. 2010;11(1):31-40. doi: 10.1111/j.1467-789X.2009.00579.x.
9. Longo M, Zatterale F, Naderi J, Parrillo L, Formisano P, Raciti GA, et al. Adipose Tissue Dysfunction as Determinant of Obesity-Associated Metabolic Complications. Int J Mol Sci. 2019;20(9):2358. doi: 10.3390/ijms20092358.
10. Padwal RS, Pajewski NM, Allison DB, Sharma AM. Using the Edmonton obesity staging system to predict mortality in a population-representative cohort of people with overweight and obesity. CMAJ. 2011;183(14):1059-66. doi: 10.1503/cmaj.110387.
11. Wharton S, Lau DCW, Vallis M, Sharma AM, Biertho L, Campbell-Scherer D, et al. Obesity in adults: a clinical practice guideline. CMAJ. 2020;192(31):875-91. doi: 10.1503/cmaj.191707.
12. Bray GA, Greenway FL. Current and potential drugs for treatment of obesity. Endocr Rev. 1999;20(6):805-75. doi: 10.1210/edrv.20.6.0383.
13. Ministry of Health of Ukraine. Unified clinical protocol (primary, secondary specialized) medical care for non-alcoholic steatohepatitis. 2014. Order No. 826. 2014 November 06. 28 p.
14. Ministry of Health of Ukraine. Treatment of obesity. Guidelines on the principles of evidence-based medicine [Internet]. Guideline No. 00500. Kyiv: Ministry of Health, DUODECIM MedicalPublications, Ltd.; 2017. Available at: https://guidelines.moz.gov.ua/documents/3336.
15. Mechanick JI, Hurley DL, Garvey WT. Adiposity-based chronic disease as a new diagnostic term: the american association of clinical endocrinologists and american college of endocrinology position statement. Endocr Pract. 2017;23(3):372-8. doi: 10.4158/EP161688.PS.
16. Obesity Canada. First Update to 2020 Adult Clinical Practice Guidelines [Internet]. Edmont: Li Ka Shing Centre for Health Research Innovation University of Alberta; 2022. Available from: https://obesitycanada.ca/guidelines/.
17. North American Association for the Study of Obesity National Heart Lung and Blood Institute; National Institutes of Health (U.S.) NHLBI; Obesity Education Initiative. The Practical Guide: Identification Evaluation and Treatment of Overweight and Obesity in Adults [Internet]. Bethesda Md: NHLBI; 2000. 94 p. Available from: https://www.nhlbi.nih.gov/files/docs/guidelines/prctgd_c.pdf.
18. Batsenko D, Braginskyi P, Buchma M, Horoshko A, Gutsalova H, Gurin M, et al. How to organize a system of providing primary medical care at the local level. Operational manual [Internet]. Kyiv: Ministry of Health; 2018. 368 p. Available from: https://medplatforma.com.ua/files/news-medsprava/2523/operatciyne_kerivnytctvo.pdf.
19. Ministry of Health of Ukraine. The role of motivational interviewing in treatment and lifestyle modification Guidelines based on evidence-based medicine [Internet]. Guideline No. 01142. Kyiv: DUODECIM MedicalPublications, Ltd.; 2017. Available at: https://guidelines.moz.gov.ua/documents/3853.
20. Yumuk V, Tsigos C, Fried M, Schindler K, Busetto L, Micic D, et al. Obesity Man-

agement Task Force of the European Association for the Study of Obesity. European Guidelines for Obesity Management in Adults. Obes Facts. 2015;8(6):402-24. doi: 10.1159/000442721.
21. Mayer SB, Graybill S, Raffa SD, Tracy C, Gaar E, FACS, Wisbach G, et al. Synopsis of the 2020 U.S. VA/DoD Clinical Practice Guideline for the Management of Adult Overweight and Obesity. Mil Med. 2020;1;186(9-10):884-96. doi: 10.1093/milmed/usab114.
22. McCulloch J, Ramesar S, Peterson H. Psychotherapy in primary care: the BATHE technique. Am Fam Physician. 1998;57(9):2131-4.
23. Arkowitz H, Miller WR, Rollnick S. Motivational interviewing in the treatment of psychological problems (2nd ed.). New York: The Guilford Press; 2015. 389 p.
24. Hugo K. Motivational Interviewing and Field Instruction: The FRAMES model. J Marital Family Therapy. 2012; 23:203-15.
25. Hashemzadeh M, Rahimi A, Zare-Farashbandi F, Alavi-Naeini AM, Daei A. Transtheoretical Model of Health Behavioral Change: A Systematic Review. Iran J Nurs Midwifery Res. 2019;24(2):83-90. doi: 10.4103/ijnmr.IJNMR_94_17.
26. Mastellos N, Gunn LH, Felix LM, Car J, Majeed A. Transtheoretical model stages of change for dietary and physical exercise modification in weight loss management for overweight and obese adults. Cochrane Database Syst Rev. 2014;(2):CD008066. doi: 10.1002/14651858.CD008066.pub3.
27. Whitlock EP, Orleans CT, Pender N, Allan J. Evaluating primary care behavioral counseling interventions: an evidence-based approach. Am J Prev Med [Internet]. 2002;22(4):267-84. doi: 10.1016/s0749-3797(02)00415-4.
28. Sherson EA, Jimenez EY, Katalanos N. A review of the use of the 5 A's model for weight loss counselling: differences between physician practice and patient demand. Family Practice. 2014;31(4):389-98. doi: 10.1093/fampra/cmu020.
29. Worl Health Organisation. Waist Circumference and Waist-Hip Ratio Report of a WHO Expert Consultation [Internet]. Geneva: WHO; 2008 47 p. Available from: file: http://apps.who.int/iris/bitstream/handle/10665/44583/9789241501491_eng.pdf? sequence=1.
30. Ministry of Health of Ukraine. Unified clinical protocol of primary, secondary (specialized) and tertiary (highly specialized) medical care prevention of cardiovascular diseases. 2016. Order No. 564. 2016 June 13. Kyiv: Ministry of Health; 2016. 18 p.
31. Patriquin MA, Mathew SJ. The Neurobiological Mechanisms of Generalized Anxiety Disorder and Chronic Stress. Chronic Stress (Thousand Oaks). 2017;1:2470547017703993. doi: 10.1177/2470547017703993.
32. Zagayko A, Shkapo A, Bryukhanova T. Study of mechanisms of influence of hydroxycitric acid on brain serotonin content under conditions of a high-calorie diet in rats. In: Material VII Nat. congress pathophysiologists of Ukraine from international with the participation of Pathophysiology and pharmacy: ways of integration; 2016 October 5-7; Kharkiv. Kharkiv: NFaU Publishing House; 2016, p. 88.
33. Hodge S, Bunting BP, Carr E, Strain JJ, Stewart-Knox BJ. Obesity, whole blood serotonin and sex differences in healthy volunteers. Obes Facts. 2012;5(3):399-407. doi: 10.1159/000339981.
34. Tavares GA, Torres A, de Souza JA. Early Life Stress and the Onset of Obesity: Proof of MicroRNAs' Involvement Through Modulation of Serotonin and Dopamine Systems' Homeostasis. Front Physiol. 2020;11:925. doi: 10.3389/fphys.2020.00925.
35. Froy O. Circadian rhythms and obesity in mammals. ISRN Obes. 2012;2012:437198. doi: 10.5402/2012/437198.
36. Namkung J, Kim H, Park S. Peripheral Serotonin: a New Player in Systemic Energy Homeostasis. Mol Cells. 2015;38(12):1023-8. Available from: doi: 10.14348/molcells.2015.0258.
37. Voigt JP, Fink H. Serotonin controlling feeding and satiety. Behav Brain Res. 2015;277:14-31. doi: 10.1016/j.bbr.2014.08.065.
38. Flores RA, da Silva ES, Ribas AS, Taschetto APD, Zampieri TT, Donato J Jr, et al. Evaluation of food intake and Fos expression in serotonergic neurons of raphe nuclei after intracerebroventricular injection of adrenaline in free-feeding rats. Brain Res. 2018;1678:153-63. doi: 10.1016/j.brainres.2017.10.021.
39. Anderberg RH, Richard JE, Eerola K, López-Ferreras L, Banke E, Hansson C, et al. Glucagon-Like Peptide 1 and Its Analogs Act in the Dorsal Raphe and Modulate Central Serotonin to Reduce Appetite and Body Weight. Diabetes. 2017;66(4):1062-73. doi: 10.2337/db16-0755.
40. Versteeg RI, Koopman KE, Booij J, Ackermans MT, Unmehopa UA, Fliers E, et al. Serotonin Transporter Binding in the Diencephalon Is Reduced in Insulin-Resistant Obese Humans. Neuroendocrinol. 2017;105(2):141-9. doi: 10.1159/000450549.
41. Sridhar GR, Lakshmi G. Sleep, obesity and diabetes: the circadian rhythm. Advances in diabetes: newer insights. In: Sridhar GR (Ed), editor. New Delhi: The health Services Publisher; 2016, pp. 196-207. doi: 10.5005/jp/books/12744_16.
42. Sridhar GR, Sanjana NS. Sleep, circadian dysrhythmia, obesity and diabetes. World J Diabetes. 2016;7(19):515-22. doi: 10.4239/wjd.v7.i19.515.
43. Hannon J, Hoyer D. Molecular biology of 5-HT receptors. Behav Brain Res. [Internet]. 2008;195(1):198-213. doi: 10.1016/j.bbr.2008.03.020.
44. Kim H, Toyofuku Y, Lynn FC, Chak E, Uchida T, Mizukami H, et al. Serotonin regulates pancreatic beta cell mass during pregnancy. Nat Med. 2010;16(7):804-8. doi: 10.1038/nm.2173.
45. Kim K, Oh CM, Ohara-Imaizumi M, Park S, Namkung J, Yadav VK, et al. Functional role of serotonin in insulin secretion in a diet-induced insulin-resistant state. Endocrinol. 2015;156(2):444-52. doi: 10.1210/en.2014-1687.
46. Zagrebaeva OYu. The role of the serotoninergic system in the development of obesity. Medical news. 2016;4(259):15-7.
47. Bassols J, Prats-Puig A, Vázquez-Ruíz M, García-González MM, Martínez-Pascual M, Avellí P, et al. Placental FTO expression relates to fetal growth. Int J Obes (Lond). 2010;34(9):1365-70. doi: 10.1038/ijo.2010.62.
48. Obradovic M, Sudar-Milovanovic E, Soskic S, Essack M, Arya S, Stewart AJ, et al. Leptin and Obesity: Role and Clinical Implication. Front. Endocrinol. 2021;12:585887. doi: 10.3389/fendo.2021.585887.
49. Izquierdo AG, Crujeiras AB, Casanueva FF, Carreira MC. Leptin, Obesity, and Leptin Resistance: Where Are We 25 Years Later? Nutrients. 2019;11(11):2704. doi: 10.3390/nu11112704.
50. Schepers J, Gebhardt C, Bracke A, Eiffler I, von Bohlen Und Halbach O. Structural and functional consequences in the amygdala of leptin-deficient mice. Cell Tissue Res. 2020;382(2):421-6. doi: 10.1007/s00441-020-03266-x.
51. Guo M, Lu Y, Garza JC, Li Y, Chua SC, Zhang W, et al. Forebrain glutamatergic neurons mediate leptin action on depression-like behaviors and synaptic depression. Transl Psychiatry. 2012;2(2):e83. doi: 10.1038/tp.2012.9.
52. Boryak KH. Determining the impact of weight gain at a young age on the quality of life. Herald of problems of biology and medicine. 2019;2(154):390-4. doi: 10.29254/2077-4214-2019-4-2-154-390-394.
53. Mach F, Baigent C, Catapano AL, Koskinas KC, Casula M, Badimon L, et al. 2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk. Eur Heart J. 2020;41(1):111-88. doi: 10.1093/eurheartj/ehz455.

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