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Is Physical activity an effective tool to reduce depression after coronary artery event?

A Systematic Review

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ABSTRACT

Background

In most countries of the Western world there have been positive reductions in incidence of cardiovascular diseases in the past decades, among both men and women, but still mortality due to these disease groups are very high. Many studies about myocardial infarction have shown that depression after an event is related to poor medical outcomes from the disease. This means prolonged disability events of angina, arrhythmias, re-hospitalization and increased rate of mortality. In post myocardial infarction patients, depression is a major cause of both short and long term mortality.

Aim

The aim of this study was to examine the scientific literature by a systematic review in order to find evidence based knowledge about the benefit of physical activity as a tool to reduce depression in patients with coronary artery event.

Method

Three databases were searched (Pubmed, CINHAL, Cochrane) systematically and all articles that met inclusion criteria were examined and graded according to the criteria "Grading quality of evidence and strength of recommendations" by Atkins. A special protocol was designed further from AMSTAR by Beverley, for systematic review with and without the meta-analysis study.

Results

It was evident that scientific reports fitting to the area was scarce showing that the area of interest was fairly new. Finally ten studies were included in this study, one meta-analysis, five randomized controlled trail and four clinical trials.

The results showed low to moderate evidence for the use of high, moderate and low level of exercise as a tool to reduce depression in post coronary artery event patients.

Conclusion

The following study concluded that, exercise shows positive effects to reduce the level of depression among coronary artery event patients.

Keywords: Aerobic exercise**,** Coronary artery disease, Depression, Myocardial infarction, Physical activity.

CONTENTS

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ABBREVIATION

AMI	Acute myocardial infarction
CAD	Coronary artery disease
CABG	Coronary artery bypasses surgery
CHD	Coronary heart disease
CVD	Cardiovascular disease
MDD	Major depressive disorder
WHO	World Health Organization

INTRODUCTION

Before starting this study, in the two years Master of Public Health program, I worked as a physical therapist at Aga Khan University Hospital, department of cardiac ward in Karachi, Pakistan. I understood that those patients who have/had cardiac events suddenly had to change their whole life in order to manage their new life situation. Sometimes they needed to change lifestyles i.e stop smoking, had to start a new diet and exercise plan. Some of the patient suffered from disability after debut of their disease and some might not be able to go back to working life. Many patients thereby not only suffered from the trauma they had after their event but also needed to adapt to a new life. Sometimes these patients thereby mourned the loss of their former life, felt a lower quality of their new life and would express signs and symptoms of depression. As a physiotherapist I worked in rehabilitation of this patients group. I many times wondered if the daily exercise program helped them to overcome the feeling of depression and if raised level of physical activity actually could be a tool to reduce the risk of depression in them. It is well known that depression is an important risk factor for i.e myocardial infarction and in this case re-infarction. After end of my theoretical master of public health studies I therefore decided to conduct a systematic review in order to find evidence from research on this subject since I also know that physical activity has many other positive effects on cardiovascular diseases. Furthermore, my own experiences showed that increased physical ability, increases wellbeing and self-esteem among these patients which are other important factors for the good results in rehabilitation.

BACKGROUND

In the Western world there have been seen a positive reductions in incidence of cardiovascular diseases in the past decades among both men and women, but still mortality due to these disease groups is still high. Men are affected by myocardial infarction more often than women even though the mortality rate has gone down [1]. There have been multiple interventions done to focus on what more can be done to utterly reduce the incidence of myocardial infarction and these interventions have mostly been conducted to target at reduction of the greatest preventable risk factors in the populations such as, smoking cessation, lipid reduction, regulation of hypertension, and increased exercise. These are all well-known preventable mutual risk factors for heart disease [2]. These interventions together with all more effective treatments in the acute phase in hospital ward i.e. anti-clotting medicament etc. have together resulted in a lower incidence in mortality in CVD-diseases among both genders. Still there are more to be done and examined, to utterly reduce the incidence [2].

1. Heart disease

The cardiovascular diseases are affecting the heart and all surveillance system is based on the below definitions [3]:

1.2. Classification of Heart disease

Type 1 – Sudden myocardial infarction is caused by primary coronary incident such as erosion or rupture of plaque.

Type 2 – Due to coronary embolism, coronary artery spasm, arrhythmias, anemia, hypotension or hypertension may causes ischemia, either increased or decreased demand of oxygenated blood supply and it precede to myocardial infarction.

Type 3 – Spontaneous unexpected cardiac death, including cardiac arrest with the symptoms of myocardial ischemia, evidence of fresh thrombus in a coronary artery by autopsy or angiography, or new ST elevation, or new Left Bundle Branch Block (LBBB).

Type 4 – Associated with stents or coronary angioplasty.

Type 4a – Myocardial infarction related with percutaneous coronary intervention (PCI).

Type 4b – Myocardial infarction related with stent thrombosis, which is found in autopsy or in angiography.

Type 5 – Myocardial infarction related with coronary artery bypass graft.

1.3. Coronary artery occurrence and symptoms

Coronary artery disease is also known as atherosclerotic heart disease, due to enhancement of athermanous plaque inside the walls of arteries (this plaque is form by cholesterol, fat etc) [4]. These arteries provides / and are responsible to supply the blood to myocardium with nutrition's and oxygen. Due to the accumulation of plaque in the lumen of artery it is narrowed (decrease the diameter of artery). Then it also called coronary heart disease [4].

Coronary artery disease is one of the major leading causes of death worldwide [5]. The sign and symptoms of coronary artery disease are seen after the first onset of heart attack, most persons who are suffering from coronary artery disease shows no evidence for long period until the disease enter into the advance stage and cause heart attack [6]. This disease is the most common cause for death in men and women over the age of 20 year, but are seldom seen at young age and this is the most common reason of sudden death [7,6]. According to the present life style in United States of America, one out of three women develop coronary artery disease in future and 50% of healthy men as well [8].

There is a difference between myocardial infarction and ischemia. Ischemia means "Insufficient supply of blood to the tissues of an organism according to their need". [9]. Due to ischemia the myocardium thus not perform their function normally because there is destruction in contraction and relaxation of the myocardium. Restoration of blood supply to the tissues of myocardium can revere the process of myocardial ischemia [9]. Infarction means "the tissue of an organism goes into irreversible stage or causes death due to the lack of oxygenated blood" [10].
Acute myocardial infarction (AMI) usually gives symptoms of ischemic pain, serum catalytic enzymes, systemic shock, change in electro cardio graphic (ECG), and fatal collapse [11]. The severity of arterial disease gives the results into fatal and non-fatal AMI. Silent AMI shows asymptomatic features having no changes in ECG and enzymes. Abrupt cardiac mortality arising due to the chaotic electro-muscular activity in heart, probably with varied origins to AMI. Few of the cases have complained of chest pain before AMI or sudden death [11].

Angina refers to chest pain which occurs regularly after heavy meals, activity or on predictable times and is stated as “stable angina” due to the narrowing of the walls of heart arteries at the severe stage [9].

Another type of angina is known as “unstable angina”, which changes in intensity, frequency or character. Unstable angina progress to myocardial infarction and needs an urgent medical attention [9].

1.4. Gender differences between men and women in prevalence of heart disease

There are well known differences in symptoms of myocardial infarctions between men and women and men are also at higher risk to get affected by myocardial infarction as compared to women (before the menopause) [12]. Results from a Norwegian study shows that men are 4.6 times prone to get myocardial infarction as compared to women, those women who smokes are six times more prone to get myocardial infarction. Smoking men on the other side are three times more prone to MI as compared to non-smoking men and women [13]. According to Danish researchers, they showed that women were more sensitive to tobacco use which increased the risk of myocardial infarction in current smokers and in those exposed to tobacco smoke, which made a higher prevalence in women than in men [13]. Danish researchers found that, approximately all smokers starts smoking before the age of 18 years. When smokers get into their middle ages they have experienced 9 -10 years of smoking which increases the incidence of cardiac rates among women in combination with other risk factors and in some cases there could be seen by a synergy effect when smoking get was that combined with i.e. high blood pressure [14]. Another reported difference is that women usually are struck by cardiac events later in their lives and at that time they more often are facing other diseases like hypertension, diabetes etc. Women`s mortality rate in heart disease increases after the menopause but it is still not higher than the incidence in men [15].

1.5. Mortality rate from coronary heart disease

Table 1: Mortality rate

	Low income countries		Middle income countries		High income countries		World	
	Deaths in millions	Death in %	Deaths in millions	Death in %	Deaths in millions	Death in %	Deaths in millions	Death in %
Ischemic Heart Disease (2008)	0.57	6.1%	5.27	13.7%	1.42	15.6%	7.25	12.8%

Source: WHO, 2012

1.6. Risk factors for heart diseases

1.6.1. Major Non preventable risk factors

There are some risk factors which cannot be change and thereby cannot be prevented.

Age

Age is one of the major risk factor for coronary artery disease, 82% of death attributed above the age of 65 years old due to coronary artery event [15].

Heredity and race

Children whose parents have/had heart disease have higher inherited risk. African Americans have a high prevalence of hypertension and at greater risk for heart disease as compare to Caucasians Americans. The risk of heart disease are also higher in American Indians, native Hawaiians, Mexican American and some Asian Americans, higher risk is due to the obesity and diabetes [15].

1.6.2. Major preventable risk factors

Use of tobacco

Those individuals who smoke tobacco are 2 – 4 times more prone to the risk of the coronary artery event as compare to those who don't smoke tobacco. Smoking cigarette is a strong risk factor for cardiac mortality among those who have coronary artery disease [15].

High blood cholesterol level

High blood cholesterol level increases the risk for coronary heart event. This increases the risk to greater extent if tobacco smoking and high blood pressure is also present. Age, diet and hereditary are also risk factors to raise high blood cholesterol level.

Health advice: Restrict LDL cholesterol level to less than 160mg/dl, in order to lower the risk for heart disease. For persons in the middle of high and low risk, ought to restrict their LDL cholesterol level to 130mg/dl, and for those at higher risk, then they ought to lower their level of cholesterol to 100 mg/dl.

HDL cholesterol is healthier for the body as compare to LDL. The normal level of HDL is between 40 – 50 mg/dl in both men and women.

Triglycerides cholesterol level ought to be less than 150 mg/dl to keep healthy [15].

Hypertension

Due to hypertension the cardiac muscles losses elasticity and cardiac muscle become hypertrophy due to increase in work load. This is a normal mechanism and leads heart to insufficiency. This mechanism increases the risk of incidence of myocardial infarction, stroke, congestive heart failure and kidney failure. The risk of stroke and myocardial infarction is increased more if hypertension exists with obesity, diabetes or high blood cholesterol level [15].

Physical activity and Physical Inactivity

Inactivity is one of the major risk factor for coronary heart disease. Regular physical activity or moderate to vigorous type of physical activity is beneficial for the body and decreases the risk for blood vessel disease and coronary heart event. The more you are physical active the lower the risk for coronary heart disease. Physical activity controls normal levels of blood cholesterol level, diabetes and obesity level and blood pressure [15].

Over weight and obesity

High body weight increases the risk of myocardial infarction among those individuals who are even without involving other risk factors. The work load of the heart increases by weight increase. Due to increase in work load of the heart the level of blood pressure, blood cholesterol and triglyceride increases and decreases HDL level for the body [15].

Diabetes mellitus

Diabetes mellitus increases the risk for heart disease both when it is regulated and if not. But if the glucose level is not controlled it increases the risk of heart disease utterly [15].

Socio demographic risk factors

Many studies show that, individuals who belong to low socioeconomic status have a higher risk of coronary heart disease (RR 1.3 – 2.0). They also have a higher risk of other diseases. Low socioeconomic status is defined as "Those people who have low status job, low income, having low education or living in low residential area" [16].

Stress

A recent result from the systematic review shows that, stress during work is an increasing risk factor for cardiovascular disease especially in men (OR > 1.5). Regarding women it is harder to draw a conclusion of the risk of work stress since fewer studies have been conducted. More studies on family stress have been showing that stress may increase the risk of coronary heart disease utterly (RR 2.9 – 4.0) in women [16].

Social depravation

Absence from social activates may lead to an increase in chronic stress, Recent systematic reviews concludes that those individuals who are less social activated and deprived from social communities are also more prone to die prematurely of coronary heart diseases [16].
The risk factors of CHD differ geographically and socially. Regarding prevalence of CHD in society, poor communities have higher prevalence as compare to wealthy communities [17].
In communities that have a high prevalence of low occupational status, low level of education, unemployment, substandard housing, overcrowding, a high prevalence of old senior citizens and low income also have a high prevalence of CHD. These situations might lead people to migration, delay in marriage, divorce, being without a job, take extra work and get hypertension. These situations increase the risk of CHD mortality [17].

To conclude CHD risk factors differ according to different level of social groups, already said as people living in deprived circumstances are more prone to get CHD because they face more

difficulties in their daily lives. Consequences thereby become more aversive for them and in the other hand, these problems also increases the risk of depression [17].

Exposure to depression increases due to low education, personal uncertainty, adoption of a sedentary life style, recently and change residential place, recently unemployment and chronic health circumstances. Within these conditions, depression can be cause by age, origin, marital status, health practice, income, divorce or separation. Furthermore depression is a severe risk factor of myocardial infarction [17].

2. International risk factor management program

2.1. Smoking

Many prospective cohort studies have shown benefits of smoking cessation in relation to coronary heart disease. Some studies also concluded that, after 10 years of being smoke free people reduces the risk of coronary artery disease equal to the level of those who have never smoked. A 50 years follow up study from the British study concluded that, the age has greater impact on smoking cessation. Those ex-smokers who quit smoking between the ages of 35 to 44 years have an equal survival rate as compare from those who never smoked [18].

Smoking cessation counseling usually will be conducted by physicians, nurses, health counselors and psychologists and these caregivers also need to be inquiring about the dosage of smoking. Systematic reviews regarding smoking cessation counseling shows that, regular consultations results in that 2% of smokers change into smoking cessation for at least one year [18]. Nicotine therapy also plays an important role to increase the smoking cessation rates and prevention from coronary artery disease. Nicotine can be given in the form of skin patch, nasal spray and nicotine gum and tablets [18].

2.2. Diet

2.2.1. Effects from Unsaturated fat, Saturated fat, Trans-fatty acids and cholesterol

The relationship between coronary heart disease and dietary saturated fat has been investigated comprehensively. Saturated fats are responsible to trigger the raise of LDL – cholesterol levels [18].

Studies show substitutes of saturated fat is n-6 polyunsaturated fatty acid which is found enough in sunflower oil and monounsaturated fatty acid in olive oil. This substitution helps to decrease the risk of coronary artery diseases [18].

Trans-fatty acids can be excreted from vegetables and animals and produced from unsaturated oils after the process of hydrogenation. Nutritional intake of trans-fatty acids decreases the HDL cholesterol and increases the LDL cholesterol level. Epidemiological and metabolic studies concluded that, trans-fatty acids incline the risk of coronary heart disease [18].

Studies have confirmed that, using monounsaturated and polyunsatured fats from the substitution of saturated and trans-unsaturated fats prevent from coronary heart disease events as compare to a reducing overall intake of fat. Current recommendations regarding diet are: Do not use more than to a 30% of calories in your regular diet from saturated fats, 10% calories from saturated fats and about 10% from polysaturated fat and 15% from monounsaturated fat [18].

2.2.2. Omega-3 fatty acids

The best sources to get Omega-3 fatty acids are fish oil and fish (which have docosahexaenoic acid and eicosapentaenoic acid) other sources are plant oil and certain nuts. Clinical trials and epidemiological studies prove that, Omega-3 fatty acid will be beneficial for those who are at the risk of coronary heart disease. The mechanism behind the Omega-3 fatty acid have a cardio protective role since it decrease the tendency of thrombosis, change lipid profile, and also gives antihypertensive, antiarrhythmic and antihypertensive effects [18].

2.2.3. Fruits and Vegetables

Recently 10 prospective cohort studies (Meta-analysis) have concluded that, utilization of fruits and fibers from cereals are beneficial to reduce the risk of coronary heart disease. The recommendation has been made according to the available source of evidence and it is 400 g of fruit and vegetables take into the regular diet [18].

2.3. Physical activity

It is scientific confirmed that, coronary heart disease and diabetes type 2 both are responsible for one third of all deaths in the world due to inadequate physical activity. According to

observational studies, leisure time physical activity would be beneficial to reduce the risk of cardiovascular mortality and morbidity among both men and women both in middle aged and older individuals [18].

The physiological functions in the body by physical activity are: enhances endothelial function, improve vasomotor function and vasodilatation in blood vessels, physical activity helps in weight reduction, glycemic control, progress blood pressure, and improves insulin resistance and lipid profile [18].

2.4. Body weight

Obesity is a rising problem among developed and developing countries. Prospective studies shows that, obesity and over weight is responsible for mortality and morbidity due to cardiovascular disease and is also responsible for hypertension, type 2 diabetes, less resistance to glucose and dyslipidemia [18].

Preventive programs for obesity shows a positive results, preventive programs promotes balance diet, physical activity, and behavioral interventions which shows significant reduction in diabetic incidence and weight loss among pre-diabetes [18].

2.5. International policy programs targeting cardiac health

During the last 20 years there has been a decrease rate of mortality in high income countries due to cardiovascular diseases. The success of the strategy is due to the interventions of individual health care strategies and control management programs within primary health care. The aim of these health care intervention strategies is to improve cardiovascular event and decrease the rate of incidence in cardiovascular event [1].

Tobacco Control

WHO Member States have made an agreement called the WHO Framework Convention on Tobacco Control (FCTC). It is approved by 170 countries in the world and contains together 90% of the total world population [1].

The recent results shows that the financial expenses required for implementing on WHO Tobacco control program ranges from US$ 0.10 – 0.23/ person/year in low income and low middle income countries, and US$ 0.11 – 0.72/person/year in upper middle income countries [1]. The major fund for this strategy is spend on educating people through media camping and other are low expenses goals such as, smoke free indoor environment, banning all tobacco marketing and increase in taxes on tobacco products [1].

After the implementation of policies, the result shows that the goals have been achieved with a reasonable cost and in a short period of time. According to the WHO FCTC articles the results shows as:
Article 6: The price of tobacco and taxes was increased.
Article 8: Making indoor environment smoke free at places such as, transportation, restaurants, work places, and public places.
Articles 11 and 12: Educating the people from the tobacco smoking.
Article 13: Proscription on any kind of tobacco marketing [1].

Diet recommendation

WHO has developed a global policy regarding salt intake. The recommendation says that adults max intake of salt 5 grams/day. In high income countries they are focusing to reduce salt intake which is used during processed food. In low middle income countries, urban and rural areas uses excessive salt intake in their foods. Education camping must be implemented to prevent from excessive salt intake in population in order to reduce risk of CVD diseases in the world [1].

Policy for physical activity

Physical activity plays a major role to control and prevent from CVD and also helps in to maintain the body weight and prevent from obesity. According to WHO NCD Action Plan of 2008, Physical activity can be promoted through: school based agendas, approved and implementation of those policies which promotes walking and cycling importance is also pollution free environment, urban design based on promoting physical activity (e.g. stairs instead of elevators), community based agenda such as promoting and educating about physical activity through media campaign, sports activities [1].

3. Treatment of Myocardial Infarction

3.1. In hospital treatment

Due to the advancement in medical technology in the modern world, the rate of mortality from acute myocardial infarction is declined by 50%. Critical care units (CCUs) prove emergency treatment such as, immediate defibrillation and supporting from the implementation of the beneficial interventions. The administration includes IV medications and the following therapy design [19].

- Prevent and limit the size of infarction due to myocardial infarction

- Prevent from the risk of myocardial ischemia

- Restore the narrowed or blocked arteries which is responsible for myocardial infarction

Injecting Beta adrenergic blockers intravenously within four hours from the onset of pain would be beneficial treatment in acute phase and it's also continued as long term treatment. The beta blockers play an important role in acute phase of treatment to decrease the size of infarct, sudden death and mortality among those patients who have Q wave myocardial infarction. Atenolol OR Metoprolol will be beneficial among patients who having unstable angina by reducing the incidence and risk of myocardial infarction [19].

In hospital the small trails like infusion of insulin with potassium and glucose through an anti-apoptotic effect helps to decrease mortality and size of infarction [19].

ACE inhibitors and beta – adrenergic blockers are both beneficial to improve the balance between the demand of oxygen supply towards the myocardium and to restrict the infarct size. Proper fluid treatment will be beneficial for the left ventricular filling pressure for maintaining oxygen saturation, control heart rate by ignoring the stimulation of reflex sympathodrenal [19].

3.2. Surgical treatment

3.2.1. Percutaneous coronary intervention

The percutaneous coronary intervention is also known as "coronary angioplasty", this procedure is used as an emergency treatment. This procedure must be done within 12 hours after the coronary artery event. The objective is to open blocked or narrowed vessels which are

responsible to carry oxygenated blood towards the myocardium [20]. Balloon catheter will be inserted along with the stent from groin or wrist region with the help of surgical guide wire. The stent get extended after inflation of balloon, to widen the narrowed artery by crushing the fatty deposition which increases blood flow in affected artery. Stent remain placed inside the artery to keep open. Stent is small in size and made up of metal. Patient discharges from the hospital within two days after the procedure of angioplasty [20].

3.2.2. Coronary Artery Bypass Graft

In this procedure a blood vessel is taken from a different part of the body, especially from the leg or chest and this additional vessel will be place above or below the blocked or narrowed coronary artery. That additional vessel is called a graft. The graft diverted the flow of blood towards the myocardium which is blocked by the occluded coronary artery [21].

4. Cardiac Rehabilitation after Myocardial Infarction

According to the studies, cardiac rehabilitation are enclosed with useful benefits, such as increasing in functional capacity, exercise tolerance, enhanced management of metabolic risk (body weight, cholesterol, blood pressure) and enhancement in wellbeing and quality of life [22].

Cardiac rehabilitation is based on exercise training programs with health education to modify risk factors, health education with the bunch of nutrition knowledge, to promote healthy life style and medical information [22].

Cardiac rehabilitation is a long term rehabilitation program, which depends on prescribed exercises, education and counseling of the patients, in order to increase the cardiac function and decrease the risk of cardiac illness, re-infarction and sudden death. Further to stabilize the atherosclerotic process or make it into the reverse direction and control cardiac symptoms. Generally a cardiac rehabilitation program is prescribed to those patients who have had myocardial infarction, coronary artery bypass surgery or have chronic stable angina [22].

The cardiac rehabilitation definition is modified by the cardiac rehabilitation team of European society of cardiology (ESC), it states as “The sum of interventions required to ensure the best physical psychological and social conditions so that patients with chronic or post acute cardiac disease may, by their own efforts, preserve or assume their proper place in society” [23].

4.1. Phases of cardiac rehabilitation

4.1.1. Inpatient rehabilitation (Phase I)

Duration period for Phase I start's from day one to fourteen days after hospital admission, those who experienced acute cardiac events or underwent to cardiovascular invasive procedure [24]. Rehabilitation in Phase I consist on individual's basis usually but in some hospitals, additionally it consists on group of patients. The protocol of Phase I cardiac rehabilitation can differ from one hospital to another. The shorter stay of patient in hospital due to acute myocardial infarction today is about 1 day after coronary angioplasty, and 5-7 days after CABG (Coronary artery bypass surgery). Due to shorter stay in the hospital, it is more difficult to manage Phase I cardiac rehabilitation program within the hospital ward [23].

To make patient ready for self-care after discharge, inpatient rehabilitation is restricted to early mobilization and brief education or counseling is given to patient to make patient aware from the risk factors and inform about future progress and follow-up visits [23].

4.1.2. Ambulatory outpatient rehabilitation (Phase II)

Phase II cardiac rehabilitation is the most monitored phase because patient in a convalescent stage and discharge plan depends on patient's progress. The exercise plan is move into advance stage than Phase I and exercise intensity is gradually increases according to the patient progress [24].

Phase II starts a few days after the discharge from hospital. In Australia and in other countries, the time period of phase II cardiac rehabilitation program is about two to three months after the acute event. But the duration time depends on the period of recovery. In United States of America, the time period of phase II cardiac rehabilitation program is about thrice in a week for 12 weeks, for those who have a health insurance. In Canada the duration of phase II cardiac rehabilitation program is about six to eight weeks, but in Europe they offer a brief period in phase II cardiac rehabilitation program, it is about 3 to 4 weeks especially in Germany [23].

The intensity of exercise level is different between countries. In United States of America and Europe the intensity of exercise are between moderate to higher level. In Australia and New Zealand they offer low to moderate level of intense exercise. United Kingdom changed their

protocol of exercise from moderate or high intensity to low level of intense exercise just as Australia [23].

4.1.3. Intermediate and Maintenance Phase III

Phase III is divided into intermediate and maintenance phase.

The phase III cardiac rehabilitation is also an ambulatory program which having a setting of less supervision [24].

The phase III cardiac rehabilitation is offering more variations in exercise training then the other phases of program. In this phase, patient obtains further exercises training, education, social support, medication and behavioral interventions [24].

The maintenance phase is plan according to the individual medical needs and fitness outcome [24]. A number of patients register in specific groups of exercise for specific reasons, such as: obese patients are registering them self to reduce the obesity through exercise, Diabetes mellitus patients, Smoking, Hypertension, Heart failure, Lipid disorder [23].

5. Physical Activity

General definition of physical activity is stated as "Any type of movement which leads to increase energy expenditure through muscle activity such as exercise, physical training, walking, outdoor activity, gardening etc. [25]

WHO recommendation of physical activity in different age levels

- Individuals aged between 18 – 64 years, are recommend to have to do moderate intensity of physical activity for at least 150 minutes or vigorous intensity aerobic exercise for 75 minutes throughout the week.
- Muscle strengthening exercises should be performed, two days in a week or more than that.
- For superfluous health benefits, adults can perform a moderate intensity of physical activity for 300 minutes in a week or vigorous intensity of aerobic exercise for 150

minutes in a week or with the combination of moderate to vigorous intensity exercise [26].

WHO recommendation for individuals over the age of 64

- To spend at least 150 minutes on moderate level of physical activity per week and 75 minutes on high level of physical activity per week.
- The duration of time per week and intensity should be gradually increased for additional health benefits.
- Muscle strengthening exercises should be performing at least twice a week.
- Those individuals who are above the age group of 65 years and have a poor mobility, they should have to perform stability exercises at least thrice in week or those exercises which enhances their balance and prevent them from falls [26].

6. Depression

According to WHO, depression disorder affects more than 350 million people all over the world [27]. Mostly depressed patients are found to have chronic conditions as compared to those who don't have chronic conditions [28].

Depressed episodes are classified as International classification of Disease 10^{th} Revision (ICD – 10) and Diagnostic and statistical manual of mental disorder (DSM – IV) for severity [29].

Table 2: Classification of depression severity

Severity Criteria	ICD-10	DSM-IV
Mild	2 typical symptoms + 2 other core symptoms	5 core symptoms + minor social/occupational impairment
Moderate	2 typical symptoms + 3 + other core symptoms	5 + core symptoms + variable degree of social / occupational impairment
Severe	3 typical + 4 + other core symptoms	5 + core symptoms + significant social/occupational impairment

Source: Oxford Handbook of Psychiatry 2004

6.1. Mood disorder

Mood is defined as "A pervasive and sustained emotion that, in the extreme, markedly affects the person's perception of the world and ability to function adequately in society" [30].

Two types of mood disorders are generally recognized, Depressive disorder/major disorders (MDD), Bipolar disorder. The other forms of depression are dysthymic disorder and cyclothymiacs disorder (BD), but these are less severe [31].

6.2. Major depressive disorders

When patient experiences one or more than one episode of major depression then he/she will be diagnosed as MDD. MDD is also known as unipolar depression, clinical depression or most commonly known as major depression. If the patients experience a single episode of MDD, then they will be diagnosed as having MDD (single episode) but if the patient experience's more than one episode of MDD then it will be diagnosed as MDD (Recurrent). And if these depressive disorders are without the periods of mania then is called as unipolar depression, because mood remains in one emotional state or "pole" [32].

A depressed patient shows a following physical indication: tiredness, headache, digestive problems, decrease of appetite, weight loss due to decrease of appetite and occasionally increases

of appetite and weight gain due to increase of appetite. Often depression coexist with physical disorders which are common in elderly people such as; stroke, cardiovascular disease, Parkinson's disease, Chronic Obstructive Pulmonary Disease [33].

In severe stage of depression the patient shows the symptoms of psychosis, the symptoms are known as: delusion, hallucination (less common), unpleased, poor concentration [34]. Other symptoms of MDD include poor attentiveness, loss of memory especially in those patients who have the psychotic and melancholic features [35]. Recurrent thoughts of death and suicide, deprived from social communities and social activates, reduced sex drive [34]. Insomnia is frequently found among depressed patients and having the prevalence of 80% among MDD patients. Hyper insomnia is also prevalent among few MDD patients [34].

Psychosis: It is an abnormal condition of the human psyche; the term psychosis is a generic name for mental state. This is briefly described as "Loss of contact with reality" [36].

6.3. Bipolar disorder

BD is known as "Manic depression" also known as mood disorder. It's illustrated by irregular phases of mania and depression (in addition to some cases of rapid cycling, psychotic indication and mixed states) [37].

Mania: It is opposite of depression and shows as irritable or elevated mood, arousal. The meaning of mania is "madness, frenzy" [38].

Dysthymia: Is a chronic condition, but represent as a low mood disturbance, and the individual complain for low mood disturbance approximately every day over a period of at least two years. The symptoms are less severe than MDD, but the patient of dysthymia is prone to MD [39].

Cyclothymia: Is the subtype of bipolar disorder, consisting of repeated hypo manic and dysthymic periods, but without the full episodes of major depression and mania [37].

7. Physiological and Psychological effects of Exercise

7.1. Physiology of an Exercise

According to the physiological point of view, there are two types of physical activity an aerobic and Anaerobic. An aerobic exercise depends on oxygen for a longer duration. Anaerobic are not dependent on oxygen and for short duration. In aerobic exercise muscles acquire their energy from the oxygen dependent degradation of fat and carbohydrates. In anaerobic exercise these are for short duration exercise, muscles acquire their energy without sufficient oxygen supply which is called anaerobic metabolism. In this mechanism energy is produced by splitting glucose and glycogen and form lactic acid. So the effects of both exercise and condition of both exercises are different from one another [25].

Aerobic exercise are performed for long duration that triggers the heart and skeletal system to adopt the aerobic system, because of that aerobic exercises enhances the heart capacity due to the increase in mitochondrial volume which is engaged in the skeletal muscle cells [25].

Anaerobic exercises are performed for short duration of time which directly enhances to the muscle of heart and their function, it also important to enhance lactic acid tolerance and lactic acid production [25].

Our regular life depends on both aerobic and anaerobic physical activity such as strengthen exercise, walking in hilly area, walking, jogging etc. Usually anaerobic and aerobic exercises perform with the combination to enhance the period of time for a long time and to enhance the aerobic system of muscles and heart [25].

7.2. Exercise and Mental Health

There are three types of exercises which give immediate effects on mental health:

- Aerobic exercise
- Anaerobic exercise
- Flexibility, co-ordination and relaxation

Yoga is another example that can be conducted in order to improve muscles co-ordination, flexibility and relaxation [40].

Aerobic and Anaerobic exercises work as a stimulus which provokes physiological mechanism in brain lead to increase sympathetic tone [40].

Vigorous exercise changes the mood of healthy individuals who exercises regularly, as immediate effect they feel euphoric and become less prone to get depressed, angry or anxious. The level of anxiety reversed after exercising up to five hours. Lower level of anxiety can this way be maintained by performing exercise for least thrice a day [40].

The cardiac output increases up to five folds from 5 L/min to 25 L/min during high level exercise and the blood flow redirect to the muscles. Due to this, there is a two fold increase in cerebral blood flow. On the other in depression there is a decrease of cerebral blood flow in both hemispheres of brain [40].

Due to exercise the regional cerebral blood flow increases the level of metabolism and neural activity and as well as according to the studies, there is an evidence of hyperactivity of frontal and right posterior vacuolization among depressed patients [40].

7.3. Long term physiological effect from aerobic exercise

Physiological changes occur after the six to eight weeks of aerobic exercise. The recommendation for this change limited for those who do 60-70% of maximal aerobic exercise for 20 minutes, three times a week. Generally the effectiveness of oxygen blood supply increased due to the increased in muscle blood flow and stoke volume. Physiologically it works due to the stimulation of the sympathetic activity, change in hormonal level from the same physical activity recommendation. Adaptation and change in hormonal levels is mediated by hypothalamic pituitary adrenal axis after the regular exercise [40].

7.4. Mood change mediator

The brain monoamines are responsible to play their role as a mediator of change in mood. Regarding depressed patients, the central monoamine metabolism is disrupted along secondary

patients; the decrease metabolism is due to either serotoninergic or noradrenergic system. The brain monoamines are activated by the effect of ECT and anti-depressant procedure [40].

7.5. Benefits of exercise on psychology

According to the benefits of exercise on psychology, exercise gives a cathartic function towards the hostility, anger and emotion which is responsible for self in depression. Exercise provides defensive mechanism by sublimation [40].

Among regular runner, exercise support to change their negative thoughts. In short term it diverts the depressive thoughts and support to retrieve the positive memory. However exercise supports to change maladaptive thinking for a short time but frequently it can't change maladaptive thinking permanently [40].

7.6. Depression and cardiac rehabilitation

Many studies in myocardial infarction have shown that, depression is related to poor medical outcomes, which includes: prolonged disability, angina, arrhythmias and re-hospitalization due to severe completion leads to mortality [41,42].

In post myocardial infarction patients, depression is a major cause of short and long term mortality. According to the short term mortality, 222 myocardial infarction survivors was observed and concluded that, those patients suffering from major depression had a fourfold higher risk of mortality after six months as compare to non-depressed patients [43].

According to the Ziegelstein *et al*, there was a 26.5% increased mortality rate in the first four month in post myocardial infarction depressed patients as compared to only 7.3% in non-depressed [44].

Regarding long term mortality, 896 post myocardial infarction depressed patients was observed for 1 year, 18 months and 5 years. It was concluded a significant increased risk of mortality among both men and women after adjusting demographic and relevant medical risk factors [43].

7.7. Prevalence of depression in cardiac rehabilitation

There is a high prevalence of depression among CHD patients. According to the study of Rozanski *et al*, it is a threefold greater incidence of depression among the patients of CHD as compare from general population. Other study shows that, almost half of the patients experienced minor and major depression during the rehabilitation from myocardial infarction. The prevalence of major depression among hospitalized patients with myocardial infarction is about 15-20% as compared to less than 3% of prevalence in community samples [43].

Some studies evaluate the prevalence of depression among patients in cardiac rehabilitation by using psychiatric interviews. In the study by Todaro (2005) it was concluded that 9.1% were suffering from major depression and 6.4% from minor depression among 110 cardiac participants [43].

According to the DSM IV depression scale, the prevalence of depression among 61 cardiac rehabilitation participants is around 9.8% with major and 1.6% minor depression [43].

8. AIM

The aim of this study was to examine the scientific literature by a systematic review in order to find evidence based knowledge about the benefit of physical activity as a tool to reduce depression in patients with coronary artery event.

- Can physical activity decrease the level of depression among patients who have had coronary artery event?

- What optimal level and type of physical activity would be needed to decrease depression?

9. Methodology

The aim and search strategy is based on the PICO structure [45]. “P” stands for population, “I” for intervention, “C” for comparison and “O” for outcome.

Population – Individuals with coronary artery event with the age of 30 – 70 years. The age group was extended from 30- 65 to 30 – 70 years of age group, due to very few articles was found after searching systematically.

Intervention – Promotion of physical activity. Physical activity is stated as "Any type of movement which leads to increase energy expenditure through muscle activity such as exercise, physical training, walking, outdoor activity, and gardening."

Comparison – Comparison were made between the exercise with or without other treatment (counseling, stress management) versus usual care or with and without established treatment (e.g. group counseling).

Outcome – Level of depression after performing physical activity.

Inclusion Criteria

Type of study: Studies with a study design based on non-randomized/randomized controlled trails, clinical trials, systemic reviews with and without meta-analysis, was included.

Type of interventions: Those interventions/studies which promotes physical activity (Cardiac Rehabilitation, Aerobic exercises, and Resistance exercises) on an individual level or group level.

Those interventions studies were also included that were combined with exercise such as behavioral counseling, stress management (But exercise must play dominant part on intervention).

Study population: Men and women who suffered from coronary artery diseases (such as: Myocardial infarction, Coronary Artery Bypass Grafting, Stable angina, Percutaneous Trans luminal coronary angioplasty) and suffering from depression after that incidence between the age of 30 – 70 years.

Grading Protocols for randomized controlled trails and clinical trails

The articles were graded within the studies and between the studies. The criteria for grading the evidence regards appraisal of the included studies concerning study design, study quality, consistency and directness are as follow:

Study Design

Study design was categorized into randomized controlled trail and clinical trials with the support of inductive and deductive arguments [46]. Both types of studies have different types of results. For example myocardial infarction patients were randomized to either home rehabilitation or clinical rehabilitation to decrease depression through cardiac rehabilitation [46]. And home rehabilitation implemented with the same objectives as clinical rehabilitation. After the results the evidences showed which had significant results or which had influential evidences [46].

Study quality

The study quality depends on the execution of the objectives and detailed study method. Assessing study outcomes in detail such as; concealment, blinding and follow up [46].

Consistency

The word consistency refers to the related estimation of the results across studies. Our confidence will be decreased if there is important inconsistency shown in the studies [46].

Directness

Directness measure the effect of intervention, results of outcome and people in which the study is based on. For example, if the study was based on older people, more sick or only one gender (men or women) it shows some or major indirectness based on how much the estimate will affect due to this directness. The deliberation of the directness is based on evidence according to the aim of the study [46].

Table 3: Criteria for assigning grade of evidence within the study and between the studies

Type of evidence Randomized trial = high grade Observational study = moderate grade Any other evidence or study = very low grade **Decrease grade if:** - Serious (-1) or very serious (-2) limitation to study quality - Important inconsistency (-1) - Some (-1) or major (-2) uncertainty about directness - Imprecise or sparse data (-1) - High probability of reporting bias(-1) **Increase grade if:** - Strong evidence of association – significant relative risk of >2 (<0.5) based on consistent evidence from two or more observational studies, with no plausible confounders (+1) - Very strong evidence of association – significant relative risk of >5 (<0.2) based on direct evidence with no major threats to validity (+2) - Evidence of a dose response gradient (+1) - All plausible confounders would have reduced the effect (+1)

Source: Education and debate, BMJ volume 328, 19 June 2004

Imprecise and Sparse data

Imprecise data were concerned if the confidence intervals of the results were to wide then the estimate is reliable as either an important benefits or important harms.
Sparse data was conceded if the results include just few observations or events and uninformative results [46].

After combining components

After appraisal the articles evidences they should be graded according to the level of evidence observed in the included studies. The grades were categorized into high, moderate, low or very low grades [46].

The quality of evidence was graded after considering the components. Study design, study quality, consistency, directness, imprecise and sparse data (Table 3).

High grade evidence: If the study or studies don't' have any limitations, inconsistency, indirectness and sparse or imprecise data then it remain as high grade evidence. Prospective research was improbable to alter our confidence regarding the estimate of an effect.

Moderate grade evidence: The level of evidence is decrease from high to moderate grade, if any one deficiency in outcome estimation was found such as: limitations, inconsistency, indirectness and sparse or imprecise data. Prospective research was probable to increase our confidence regarding the estimate of an effect and may also change the estimate.

Low grade evidence: The level of evidence is decreases from moderate to low grade, if limitations, inconsistency, indirectness and sparse or imprecise data were found (any two of them). Prospective research was probable to increase our confidence regarding the estimate of an effect and also change the estimate.

Very low grade evidence: If the study or studies was found with the lack of any three or all them from these outcome estimation such as: limitations, inconsistency, indirectness and sparse or imprecise data. Very uncertain effects of an estimation.

Quality assessment between the studies

- Number of patients in intervention and control group

- Calculate the mean of intervention group and control group ($\bar{x}$ 1 x population 1 + $\bar{x}$ 2 x population 2 ÷ Total Population)

- Quality of the evidence (High, Moderate, Low, Very low)

- Importance of the evidence (It based on; the evidence has any important or critical importance for making recommendations. Doesn't matter what grade of evidence they have).

Grading protocols for Systematic review and meta-analysis

Appendix 12 showe a detail description of grading protocols for systematic review and meta-analysis. That table and measurement tool assists the quality of systematic and meta-analysis reviews [47]. It consisted of 11 scores, each score contains one point and comprises the option of (Yes, No, Can't answer, Not applicable). Those answers that fall into "YES" were given one

score and except that they get zero score. The quality of evidence categorized into “Low quality” if the review get the score between 0-4, “Moderate quality” if the review get the score between 5-8 and “High quality” if the review falls into 9-11 score.

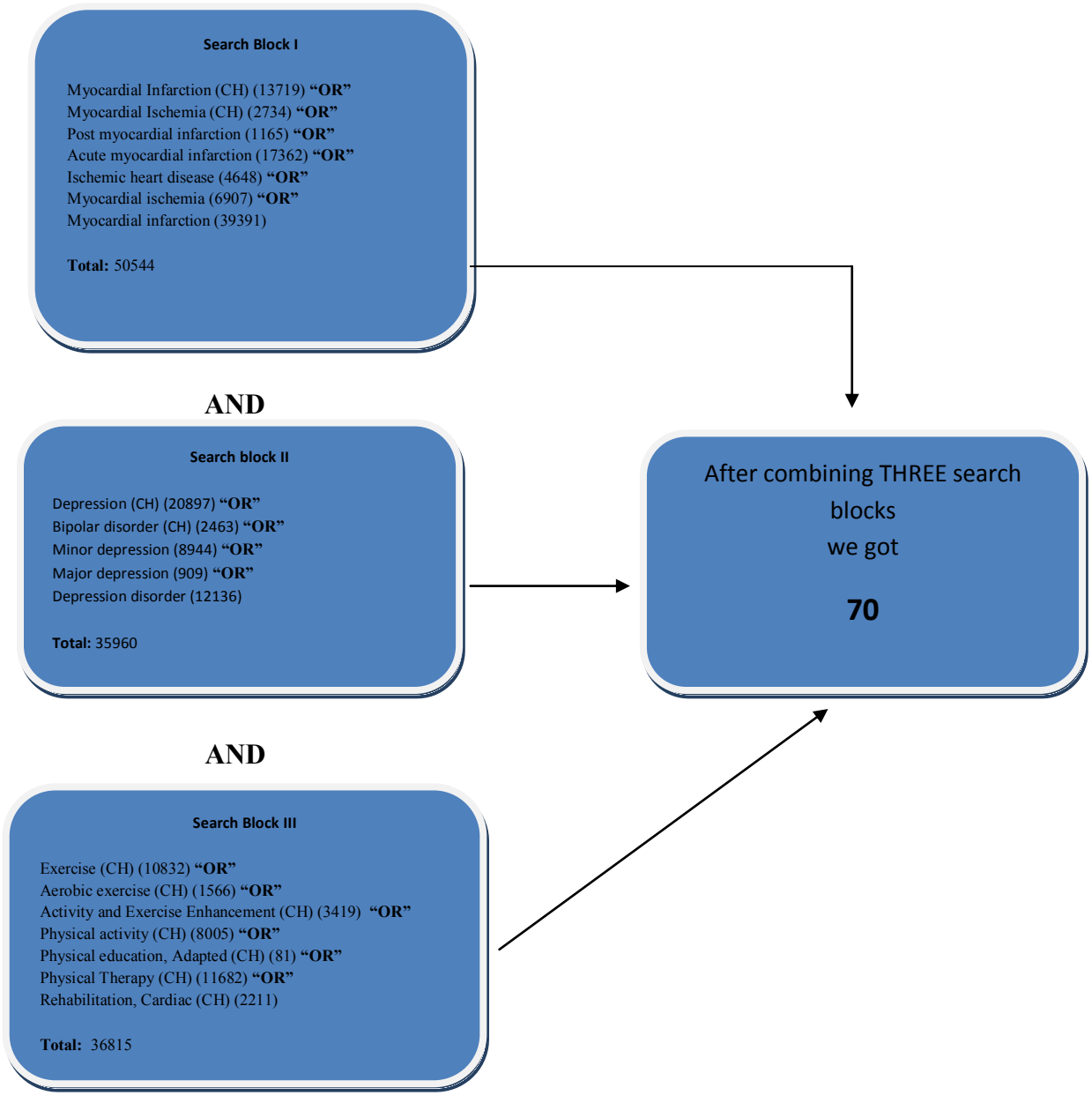
10. Search results

Following search engines were searched regarding the aim, Pub Med, CINHAL, and Cochrane Library from beginning date of the journal until 15 of May 2012. The article age limitation was eradicated due to very few number of articles was found under the articles age limit of 15 years and more than that.

CINHAL DATABASE

The result was 70 hits after merging 3 search blocks (figure 1).

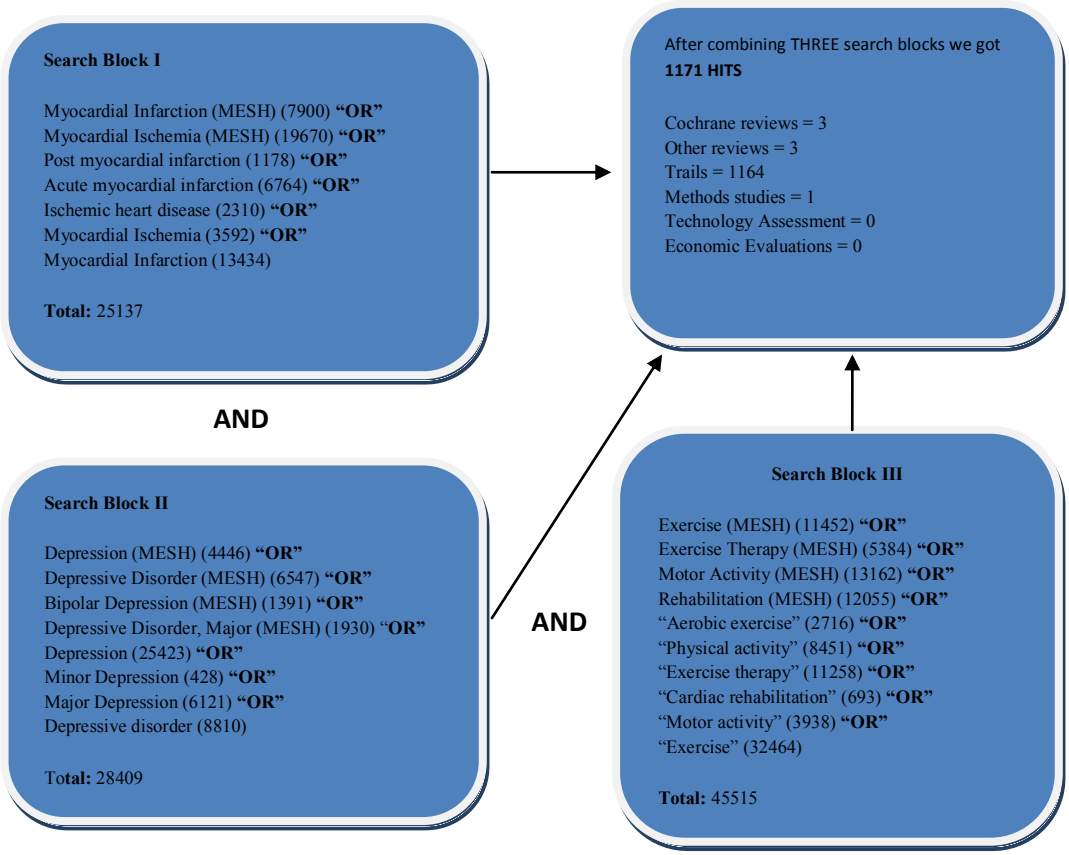
Figure 1: Search strategy in Cinhal database



COCHRANE LIBRARY

In this database was found 1171 hits (figure 2). These hits were distributed as, Cochrane reviews = 3, other reviews = 3, Trails = 1164, Methods studies = 1, Technology Assessment = 0, Economic evaluations = 0.

Figure 2: Search strategy in Cochrane database

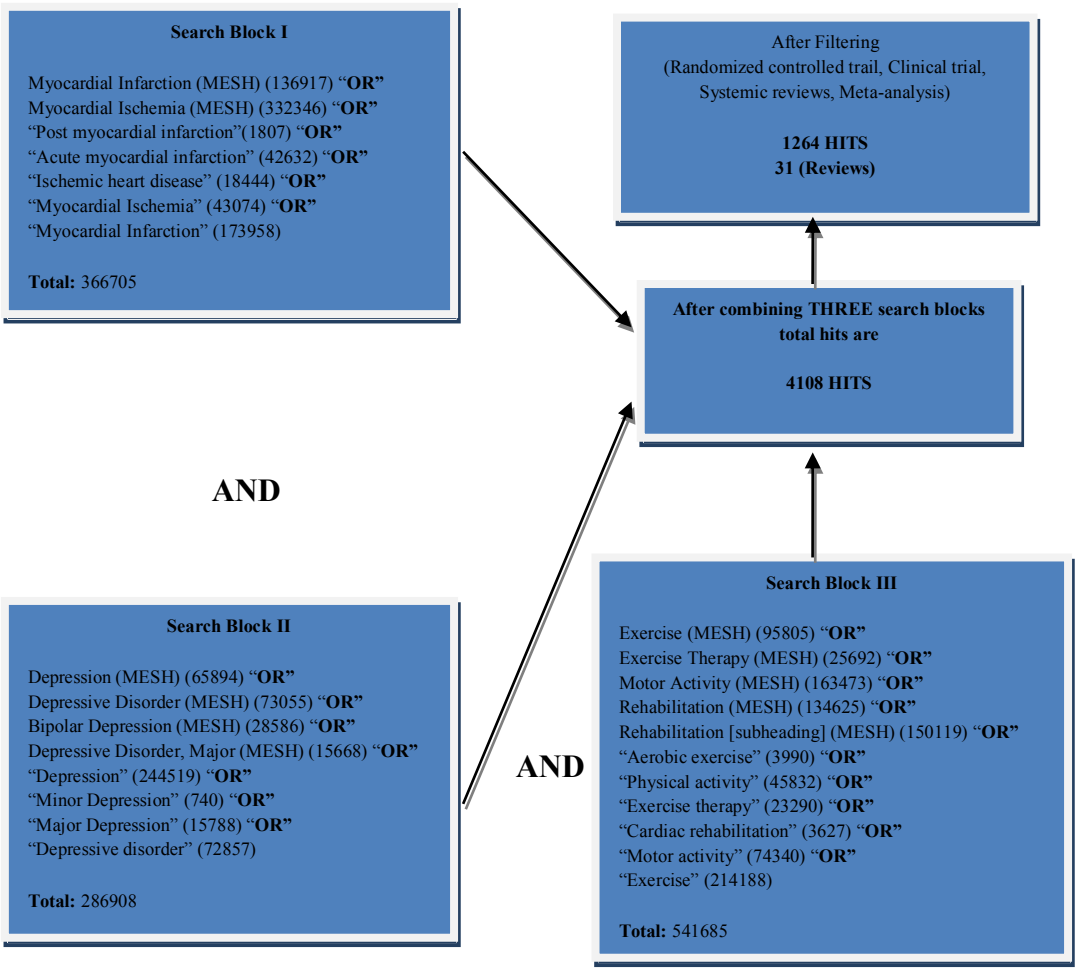


PUBMED DATABASE

Result in this database was 4108 hits on PUBMED after merging 3 search blocks (figure 3)

.

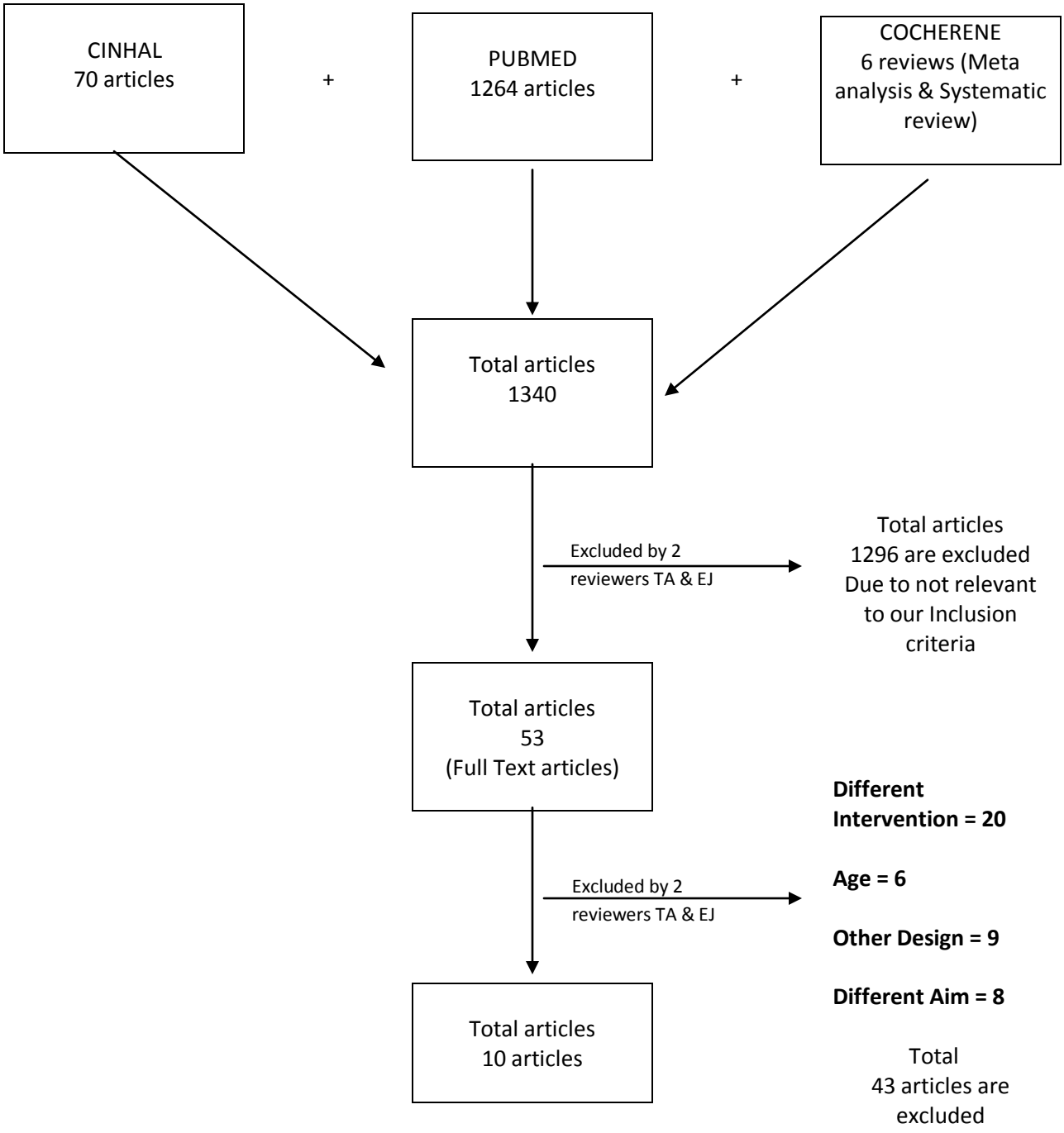
Figure 3: Search strategy in Pubmed database



11. Result

After reading 1340 abstracts and 53 articles in full text meeting inclusion criteria of the study (Fig 1) ten of them where included and 1330 were excluded (Fig 1).

Figure 4: Review Chart



Finally 10 studies were included in this study, one was a meta-analysis (Appendix 4), five were randomized controlled trail and four clinical trials. For future details concerning the content of the studies see appendix 1-3, 5-10.

The list of excluded full text articles are described in Appendix 11.

11.1. Article result

The meta-analysis study by Kugler el al [48] (Table 4) included 15 studies had the aim "To estimate the effect size of exercise treatment on depression in order to compare it with other treatments". The mean effect size was $d_{mean} = 0.4569$, which showed a medium effect of exercise on depressed patient (Appendix 4). Twelve studies were found that had control group and 3 were without. Moderate level of evidence was given according to AMSTAR criteria (see Appendix 12) [46]. Although this study included studies that had a year range from 1968 – 1991 year, the study had critical importance for making recommendations.

Table 4: Grade table of meta-analysis

	AMSTAR criteria											
Author/ Journal/year/vol	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**Total**
Kugler *et al* /British Journal of Clinical Psychology/ 1994/33	Y	C	Y	Y	Y	Y	Y	Y	Y	C	C	8

Comments: Moderate level of evidence has been given according to the AMSTAR criteria, but 3 out of 15 articles has been done without controls and that's reason for high level of patient ratio in intervention group as compared from control group. These are very old but intervention group shows a positive effect size to decrease depression and this study have critical outcome for clinical implementation.

Scale of item score: Y = Yes, N = No, C = Can't answer, NA = Not applicable

The following six exercise interventions were compared between the studies:

Exercise versus usual care (Table 5): Two studies compared exercise versus usual care, one study by Naughton *et al* [49] that had conducted a randomized clinical trial and another was a study by Taylor *et al* [50] who had a randomized controlled trial study. No limitation was reported regarding concealment, blinding or follow-up. Inconsistency between the studies was seen due to the different exercise protocols and the time duration of the intervention and follow up that were different which could lead to different estimates. Some indirectness was also seen due to absence of women in the study, although women have a high prevalence of cardiovascular disease as compare to men at older age. Data was sparse due to the absence of confidence interval reported, which make it difficult to

evaluate the reliability of the estimation between the studies. The intervention group had a decrease – 4.4 mean in depression score as compared to what was found in the control group which shows a positive results the intervention performed.

Table 5: Grade table of exercise versus usual care

Author/Year	Quality of assessment					Summary of findings						
	Design	Quality	Consistency	Directness	Other Modifying factor ‡	No of Patients		Mean*			Quality	Importance
						Intervention Group	Control Group	Intervention Group	Control Group	Mean difference		
Naughton *et al* /1978 Taylor *et al*/1986	Randomized clinical trial/Randomized controlled trial	No serious limitation	Important inconsistency	Some Indirectness	Sparse data	496	365	16.0	20.4	- 4.4	V. Low	Important

Comments: Very low level quality evidence has been given due to sparse data and inconsistency. Significant changes was shown in both studies

* Mean depression score at end of the study
‡ Imprecise or sparse data

Exercise versus Non exercise (Table 6): One study compared exercise versus non exercise [51]. These exercises were based on a low intensity exercise program. No limitation was seen, however inconsistency was seen due to the self-reporting, but some indirectness was seen due to the excluding of women, because women has high prevalence of cardiovascular disease. The data was found sparse due to the lack of reported confidence interval information which makes it difficult in the reliability of the data. The results was estimated as r = - 0.09 correlation of exercise on depression but was insignificant (Appendix 2).

Table 6: Grade table of exercise versus non exercise

Author/Year	Quality of assessment					Summary of findings						
	Design	Quality	Consistency	Directness	Other Modifying factor ‡	No of Patients		Mean*			Quality	Importance
						Intervention Group	Control Group	Intervention Group	Control Group	Mean difference		
Dorn *et al*/2001	Randomized clinical trial	No serious limitation	Important inconsistency	Some Directness	Sparse data	323	328	None	None	None	V.Low	Critical

Comments: This study based on self-report exercises evaluation the very low level of evidence and critical importance is given due to the sparse data, inconsistency and some directness.

* Mean depression score at end of the study
‡ Imprecise or sparse data

Exercise with stress management versus Usual care (Table 7): One study was included under this heading; it was conducted by Lewin *et al* [52]. No limitation was seen in the study. Important inconsistency was however seen in the study due to the combined intervention of exercise together with stress management. The study was direct in aim and objectives and reported data was found informative. The mean difference was – 1 decrease in depression score in the intervention group as compared to control group. The evidence of the study was at moderate level but it, had still important outcomes.

Table 7: Grade table of exercise with stress management versus usual care

Author/Year	Quality of assessment					Summary of findings						
	Design	Quality	Consistency	Directness	Other Modifying factor ‡	No of Patients		Mean*			Quality	Importance
						Intervention Group	Control Group	Intervention Group	Control Group	Mean Difference		
Lewin *et al*/1992	Randomized controlled trial	No serious limitation	Important inconsistency	Direct	None	88	88	3.4	4.4	- 1	Moderate	Important

Comments: The moderate level of evidence is given due to the important inconsistency

* Mean depression score at end of the study.
‡ Imprecise or sparse data

Flexibility exercise training versus Strength exercise training (Table 8): One study under this heading was conducted by Beniamini Y *et al* [53] no limitation, inconsistency and indirectness were seen in the study. Sparse data was seen due to few participants. Mean difference of – 5.7 were reported in the intervention group as compared to control group. Moderate level of evidence was found with important outcomes.

Table 8: Grade table of flexibility exercise versus strength exercise training

	Quality of assessment					Summary of findings						
Author/Year	**Design**	**Quality**	**Consistency**	**Directness**	**Other Modifying factor ‡**	**No of Patients**		**Mean***				
						Intervention Group	**Control Group**	**Intervention Group**	**Control Group**	**Mean difference**	**Quality**	**Importance**
Beniamini *et al*/1997	Randomized controlled trial	No serious limitation	No Important inconsistency	Direct	Sparse data	34	34	3.4	9.1	- 5.7	Moderate	Important

Comments: The moderate level result of evidence due to sparse data

* Mean depression score at end of the study.
‡ Imprecise or sparse data

Exercise versus group and usual care (Table 9): One study under this heading was conducted by Stern *et al* [54] no limitation, inconsistency and indirectness were seen in the study. Sparse data was seen due to lack of confidence interval that made it difficult to estimate the reliability of the result and due to few participants were found in the study. Mean difference was – 3 decrease in depression score among intervention group compared to control group and + 2.7 mean depression score was seen as compared to those in counseling group in the end of follow-up time. Moderate level of evidence was seen with important outcome.

Table 9: Grade table of exercise versus group and usual care

Author/Year	Quality of assessment					Summary of findings						
	Design	Quality	Consistency	Directness	Other Modifying factor ‡	No of Patients		Mean*			Quality	Importance
						Intervention Group	Control Group	Intervention Group	Control Group	Mean difference		
Stern *et al*/ 1983	Randomized controlled trial	No serious limitation	No Important consistency	Direct	Sparse data	42 42	64 31†	34.4 34.4	37.4 31.7*	- 3 + 2.7	Moderate	Important

Comments: The moderate level of evidence is given due to the sparse data

* Mean depression score at end of the study
† Group counseling patients
‡ Imprecise or sparse data

Exercise with group counseling versus usual care (Table 10): Three studies were included under this heading one by Engblom *et al* [55] that conducted a randomized controlled trial and two randomized clinical trials studies by Oldridge *et al* [56,57] they did randomized clinical trial design studies. No limitation was seen between studies, Inconsistency was seen due to the combined intervention of exercise together with group counseling. Directness was seen regarding aims and objectives. Sparse data was seen due to the lack of confidence interval in the studies that made it difficult to estimate the reliability of the results. Mean difference of – 0.4 among in the intervention group in depression score were reported as compared to control group. Low level of evidence was seen but with important outcomes.

Table 10: Grade table of exercise with group counseling versus usual care

Author/Year	Quality of assessment					Summary of findings						
						No of Patients		Mean*				
	Design	Quality	Consistency	Directness	Other Modifying factor ‡	Intervention Group	Control Group	Intervention Group	Control Group	Mean difference	Quality	Importance
Engblom *et al* /1997 Oldridge *et al*/1995 Oldridge *et al*/1991	Randomized controlled trial and Randomized clinical trail	No serious limitation	Important inconsistency	Direct	Sparse data	300	293	5.4	5.8	- 0.4	Low	Important

Comments: Low grade evidence was given due to the inconsistency between the studies, due to the sparse data but significant reduction in depression was seen between the studies.

* Mean depression score at end of the study
‡ Imprecise or sparse data

12. DISCUSSION

Very limited number of articles was found in three databases that associate with the aim of the study. It can be thereby assumed that, this study might have a new approach focusing on patients that are in rehabilitating post coronary event and have the complication of depression after that they have been surviving their acute face. Usually doctors and nurses might at first consider the medical, biological and the lifestyle effects in rehabilitation management. Both categories of caregivers usually do not spend as much time together with their patients as i.e. physical therapist. Furthermore as a physical therapist, you will probably see the situation of the patient in another way that will consider the effect of physical activity on the wholeness of the patient's life situations. Also physical therapist is in contact with patient for considerably longer durations during their physiotherapy session. This meeting provides an unique opportunity for the therapist to closely observe their patients physical and psychological status. They will by that have the possibility to observe not only the patients physical status but also the symptoms of mood disorders. On that background the focus of the effect of physical activity might be a new approach to lift the patients mood, and thereby their possibility of survival, as compared to the more traditional and medical thinking. It was therefore not a surprise to us that not many studies have been performed in this area. Systematic reviews on the benefits of physical activity as a tool to reduce depression in patients with coronary artery event since the approach seems to be new. However, a few studies could be found.

Prior to start the search systematically the inclusion criteria was to include those articles which had interventions of exercise without combining with other therapies such as counseling or stress management (Psychotherapy). But due to very limited number of articles it became necessary to re-formulate the inclusion criteria by also including those interventions which also combine intervention of exercise and psychotherapy.

Some of the studies did not define the age of patients in detail. It was therefore decided to include even studies that did not report standard deviation of age. In two studies, one by Beniamini *et al* [53] and one by Taylor *et al* [50] study design was not described, but after review by two reviewers (Abidi T and Janzon E) it was concluded to be a randomized controlled trail.

The included studies are conducted in different countries (United States of America, Canada, United Kingdom, Germany and Finland) among different culture and life styles with different follow-up time and different depression scales which complicate comparison across the studies. But all of the experiments are based on human beings, which can overcome this inconsistency and the reduction of depression was found in all depression scales.

Articles with exercise and/or with the combination of exercise and group counseling or exercise with stress management with usual care (control group) that showed a significant effect on decreasing the level of depression were included. However, in-significant results was shown in the study by Dorn *et al* [51] showing no correlation between exercise and depression r = - 0.09 in depression score. Still other studies showed a significant reduction in the level of depression among intervention group as compared to a usual care group in initial or later follow up's, but the reduction of depression was seen in all studies within the intervention group and with or without comparing to usual care. Regarding usual care (traditional heart disease rehabilitation care management) in some studies it showed an increase in depression score. However, some of the studies showed slightly reduction in depression after follow-up time, still not more than the intervention group (see appendix 1-3, 5-10).

Highest mean difference, highest evidence for using exercise as a tool to reduce depression, was reported in the study by Beniamini *et al* [53]. This was seen when comparing with strength versus flexibility (An exercise aim to prevent from muscular injuries by doing sport activities by elongation of muscles) in exercise training, (mean difference of – 5.7) between strength and flexibility. Lowest mean difference was calculated in exercise with group counseling (counseling helps patient to cope from maladaptive behavior, negative thoughts and emotions) versus control studies (0.4 mean differences).

The study by Stern *et al* [54], showed high mean difference, in group counseling patients as compared to the exercise group patients (difference of 2.7 mean). In the exercise group, a patient increases their work capacity; they became less depressed, less anxious, less fatigue and increases their social ability and independence in managing demands. But patients in group counseling also felt less depressed, increased in social ability, independence, and friendliness and decreased problems in their relationships, but not more beneficial than exercise group. This showed that exercise participants were at a more beneficial stage after treatment and made their

adjustment to the normal life faster as compare to the group of patients who only was treated with counseling [54].

Although exercise intervention plays an important role in the study it could not be concluded that the effect of their intervention either was due to the exercise or due to counseling or due to stress management. Sparse data sparse was seen all over the included studies except the study by Lewin *et al* [52]. Data was also sparse due to the small sample size or lack of information concerning reliability (confidence interval or standard deviation).

The meta-analysis by Kugler *et al* [48], was based on 15 studies, which concluded the effect size of exercise $d_{mean} = 0.4569$ among exercise intervention groups who had coronary artery event, which shows positive effect of exercise to reduce the level of depression among patients. Of fifteen studies three studies were conducted without controls and twelve other studies had control groups. And that's the reason that patient's ratio in intervention group was found higher than the control group (Apendix 1). However, the results shown in the study was critical in implementation of clinical outcome because the controls were of far less numbers of patients than in the intervention group and the study includes also older studies [48].

These above studies gives together an evidence that, even if we cannot say a high evidence quality, since the studies are different in their effects and results and since they were not as many as expected, physical activity can indeed be a tool to reduce depression among patients who experienced a coronary artery event. It is utterly important to understand that these patients, who actually have survived from a life crisis and thereby a trauma, can be rehabilitated by engaging into physical activity in regaining not only their physical health but also their psychological health as well. Physical activity enhances brain stimulators and lift the mood and give new energy to face life complications after myocardial and others sorts of cardiac events [56]. Furthermore, it is well known that physical activity reduces other risk factors for re-infarction and cardiac diseases i.e. diabetes, hypertension as well examined as hyperlipidemia but the effect of physical activity in reducing depression is not well examined [51].

Antidepressant medications are most frequently used as a normal treatment; but antidepressant treatment shows no effect on 30- 35 percent of depressed patients. Furthermore, antidepressant gives surplus side effects which reduce the compliance and impair the life quality of patient.

Among those patients who show a short term improvement from antidepressant medications, they are still at risk to decline the treatment within one year period and leads to termination of treatment [58].

Exercise is a suitable and alternative selection, although they have few side effects and less cost effective than the medications and other treatments such as psychotherapy [59].

The study by Paffenbarger *et al* [60] based on men concluded that, those men who were engage with three hours or more of sports activity per week, they reduces 27 percent the risk of depression as compared from those who did less than one hour per week of sports activity. The scientists found in their study, a dose response relationship between exercise and depression after combining different types of physical activity such as walking, stair climbing, sports activity. Another interesting finding was o that those who consume 2500 kcal or more during physical activity per week had 28percent less risk of developing depression as compared to those who consume 1000 kcal per week [59]. This is another interesting focus for new studies within public health.

Two meta-analysis studies on "Exercise as a treatment to reduce depression", one by Mc Donald *et al* [61] and second by Mc Cullagh *et al* [62] confirmed that exercise gave antidepressant effect.

In the study by Study by Yoshida *et al* [63] on physical and psychological improvements after phase II cardiac rehabilitation in patients with myocardial infarction. They concluded that the intervention group significantly decreased depression score (7.3 ± 4.2 versus 9.5 ± 4.2). First part of the intervention was based on warming up session which includes exercise 30-40 minutes on bicycle ergometer and stretching exercises under the supervision of physiotherapist which was performed twice a day by participants. The second part was based on 20 to 30 minutes of walking, seven days a week and twice to thrice a day. Participants in the intervention group performed anaerobic threshold (AT) exercise with 80% to 100% of heart rate (HR), which was evaluated on treadmill testing [63]. This study is not included due to the age limit (see appendix 11).

Hyperactivity has been reported in right posterior and frontal vascularization of the brain, due to exercise, and there were reported an increase in metabolism and neural activity due to increase in cerebral blood flow among depressed patients [39].

Exercise provides a defensive mechanism by sublimation process which gives anti-depressant benefits in anger, emotion and hostility which are responsible for depression [39].

13. Public Health recommendation

Three (moderate) one (low) and two (very low) levels of evidence grade studies were found in result. All of the articles has important importance for making public health recommendations except of two studies by Dorn *et al* [51] and Kugler *et al* [48] both had critical importance for making public health recommendations.

In four of the studies physical activity was combined with psychotherapy such as counseling and stress management, only six of the studies were based on exercise intervention.

For the public health recommendation point of view, physiotherapist, physicians and nurses need to be able to evaluate depression score in patients before they are discharged from hospital and during and before the time of admission into the hospital or cardiac rehabilitation. Those patient who then would be diagnosed as depressed prior to the coronary artery event or post coronary artery event, would further be recommended to undergo an evaluation of ECG more often than they apparently are having today, since depression increases fourfold risk for coronary artery disease and both diseases are bi-directional in nature [17]. Physicians needs to engage depressed patients into physical activity in rehabilitation to prevent them from experiencing a new or second artery event and also to decrease the level of depression after their event in order to fasten up rehabilitation and increase life quality of the patients. The recommendation from this study ought to be given, that the moderate level of aerobic and anaerobic exercises would be most effective.

This means that those who are suffering from depression after their coronary artery event ought to be given exercise recommendation based on aerobic exercise from phase I to Phase II rehabilitation program. This means low to moderate level of exercise combined with the partial time of counseling in educating the patient in both risk management and stress management.

Phase III exercise, which ought to be based on moderate to high level of aerobic and some form of anaerobic exercises, should be prescribed according to the condition of patient into account if he/she at discharge and still having a depression. This means that phase III rehabilitation program must be continue with the counseling days in a week even in home care three days a weeks at a gym or outdoor, at home or in outdoor.

Screening for depression

To screen depression among coronary artery event patients, a bridge is needed to be built between cardiac and psychological health care to screen the depressed patients during the course of cardiac rehabilitation or at the time of coronary artery event. Exercise therapy protocol need to be changed between caregivers, as soon as possible after the psychological screening of the patient. This enhances cardiac health as well as psychological health of patient in order to reduce the level of depression, as well as to decreases the risk of mortality and morbidity in post myocardial infarction patients. [64].

14. CONCLUSION

This study concluded that, exercise can be a useful tool to reduce the level of depression among patients who had suffered from a coronary heart event.

Physiotherapist, physicians and nurses are recommended to evaluate the score of depression in these patients during the time of admission, between the rehabilitation and before discharge. All patients who have experienced a cardiac event and shows s sign of depression ought to be engaged in moderate level of physical activity.

However, more studies are needed in this area since a majority of the found studies are old and both treatment and rehabilitation programs for patients with coronary heart events have changed rapidly during the last five years.

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16. APPENDICES

Appendix 1

Name of Author (Journal/Year/Vol)	Aim of Study/Study Design	Population (Sample/Age/Gender)	Intervention	Duration	Comparison group	Results	Grade of evidence
Beniamini *et al* (American journal of cardiology / 1997, 80)	"To assessed before and after they computed either 12 weeks of High Intensity Strength training or Flexibility training added to their outpatient cardiac rehabilitation aerobic exercise program" / Randomized controlled trial	38 (Men = 29, Women = 9) Flexibility group 16 (men = 12 and female = 4) strength 18 (men = 13 and women = 5)	Flexibility training and strength training	12 week	Flexibility training and strength training	There is a significant change in strength training from 0 week to 12 week (12.4 $\pm$ 8.9*, 3.4 $\pm$ 7.0*) P value < 0.05 and no significant change in flexibility training from 0 week – 12 week (10.3 $\pm$ 10.3*, 9.1 $\pm$ 11.3*)	Moderate

Comments: The moderate level due less number less number of observations reason for sparse data.
* Standard deviation

Appendix 2

Name of Author (Journal/Year/Vol)	Aim of Study/Study Design	Population (Sample/Age/Gender)	Intervention	Duration	Comparison group	Results	Grade of evidence
Dorn *et al* (Medicine and Science in sports and Exercise / 2001/ 33)	"Examined factors associated with exercise session compliance over 3 year in male Myocardial Infarction survival"/ Randomized clinical trail	651 men, Intervention group = 323 and Control group 328 / 30-64 years of age / Male.	"Exercise prescribed rehabilitation "First Phase (8 Week) the men exercised in a laboratory under continuous electro - cardiographe (ECG) monitoring. Participants exercised for 4 min, on six different stationary devices, with a 2 min rest interval b/w stages". "Second Phase: Participants exercised in a gymnasium or swimming pool without ECG monitoring, although exercise heart rates were periodically checked. Activities in this setting included 15 min of continuous jogging, cycling or swimming after which 25 min of recreational games were performed".	3 years follow up	Non exercising group	Katz depression score is not significant (r = -0.009) with P value = 0.11†	V.Low

Comments: This study based on self-report exercises evaluation and the very low level of evidence is given due to the sparse data, inconsistency and indirectness.
† Insignificant

Appendix 3

Name of Author (Journal/Year/Vol)	Aim of Study/Study Design	Population (Sample/Age/Gender)	Intervention	Duration	Comparison group	Results	Grade of evidence
Engblom *et al* (Journal of Cardiopulmonary rehabilitation / 1997 / 17)	"To investigate the effects of comprehensive cardiac rehabilitation after coronary artery bypass surgery (CABS)"/ Randomized controlled trail	Total population = 228 (Male = 201 and Female = 27) Intervention group = 119 (Male = 104 and Female = 15) / 54 $\pm$ 6. Control group 109 (Male = 97 and Female = 12) / 54 $\pm$ 6.	Based on exercise and counseling & comprises into four stages. **1st Stage:** Based on general information about intervention program, surgery and recovery. It starts before 2 weeks from CABS for 2 days. **2nd Stage:** It based on physical exercise, counseling for anxiety & depression, prevention of risk taking behavior regarding coronary artery disease. It starts after 6 – 8 weeks from CABS and goes for 3 weeks. **3rd Stage:** It lasted for 2 days and starts after 8 months from the CABS. Patients share their problems & experiences with the intervention team. **4th Stage:** Patent's spouses are invited for one day to share their problems and experiences after 30 months from CABS.	5 year follow up	Usual treatment	Depression scores recorded as low among intervention group as compared from control group. But the significant difference was seen between the groups after 5 year of CABS with the P value of 0.05. **Intervention group:** Mean $\pm$ SD before CABS (11.3 $\pm$ 6.8). Mean $\pm$ SD after 5 year from CABS (9.8 $\pm$ 6.0). **Control group:** Mean $\pm$ SD at before CABS (12.1 $\pm$ 7.8) Mean $\pm$ SD after 5 years from CABS (11.8 $\pm$ 7.9)	Moderate

Comments: Moderate level of evidence is given due to exercise intervention combined with conseling which shows a important inconsistency.

Appendix 4

Author/ Journal/year/vol	Aim	Number of studies	Intervention	Control group	Effect size
Kugler *et al* /British Journal of Clinical Psychology/ 33/ 1994	"To estimate the effect size of exercise treatment on anxiety and depression in order to compare it with other treatments and to define minimal group sizes for further research projects".	15	1525	389	0.4569

Appendix 5

Name of Author (Journal/Year/Vol)	Aim of Study/Study Design	Population (Sample/Age/Gender)	Intervention	Duration	Comparison group	Results	Grade of evidence
Lewin.B *et al* (The Lancet / 1992 / 339)	"To find out whether a comprehensive home – based program would reduce psychological distress" / Randomized controlled trail	176 patients Rehabilitation group (Male = 62, Female = 26) Control group (Male = 64, Female = 24) / 55.3 ± 10.7 (Rehabilitation group) Control group 56.3 ± 10.5	"Six weekly sections that included education, a home based exercise program and a tape based relaxation and stress management program"	6 week intervention and follow up for 1 year	Receives standard care plus a placebo package of information and informal counseling	**6 week:** there is a significant change between the rehabilitation group and control group. Rehabilitation group scores 3.1 ± 2.9* and control group 4.1 ± 3.5* with the P value of 0.04‡ and confidence interval of 0.1 to 2.0 **6 months:** Depression rehabilitation group 3.7 ± 3.5*, Control group 4.1 ± 4.8*, P value 0.11†, Confidence interval 0.2 to 2.4 **12 month:** Depression 3.4 ± 3.2* (Rehabilitation group), 4.4 ± 3.8* (Control group) P value 0.12†, Confidence interval 0.3 to 2.5.	Moderate

Comments: Moderate level of evidence is given due to exercise intervention combined with stress management which shows a important inconsistency.
* Standard deviation
† Insignificant
‡ Significant

Appendix 6

Name of Author (Journal/Year/Vol)	Aim of Study/Study Design	Population (Sample/Age/Gender)	Intervention	Duration	Comparison group	Results	Grade of evidence
Stern *et al* (Archives of internal medicine/ 1983 /143)	"To compare the effectiveness of two separate treatment approaches – exercise therapy and group counseling with each other and with a control group in rehabilitating psychologically and and/or physically disabled subjects following myocardial infarction" / Randomized controlled trail"	106 (Male=91 & Female = 15) Exercise intervention group = 42 (Male = 38, Female = 4), Group counseling = 35 (Male = 31, Female = 4), Control group = 29 (Male = 22, Female = 7) / Between 30 – 69 years of age.	Dynamic resistance, Upper limb exercises (rowing machine, arm ergometer, arm wheel), Lower Limb exercises (Step encounter, treadmill, cycle). The intensity of exercise changes according to heart rate with 85% of peak exercise heart rate.	12 week intervention and Follow up evaluation consists to 3 months, 6 months and one year.	**Group counseling:** Twelve sessions, 60-75 minutes weekly group counseling session under supervision of psychiatric and nurse. **Control group:** They receive usual medical care.	**3 months:** Exercise patients significantly decrease depression level by -1.40 mean changes from 34.90 mean baselines as compare from control group; mean baseline 37.33 and after 3 months mean baseline +1.00 with the P value of 0.02. **6 months:** Exercise patients decreases -1.08 mean change from the base line but not significant. **12 months:** Exercise patients shows decrease in mean change after 1 year -0.51 from mean baseline of 35.00 but not significant.	Moderate

Comments: The moderate level of evidence is given due to the small sample size and lack of information leads to sparse data.

Appendix 7

Name of Author (Journal/Year/Vol)	Aim of Study/Study Design	Population (Sample/Age/Gender)	Intervention	Duration	Comparison group	Results	Grade of evidence
Naughton *et al* (Cardiology / 1978 / 63)	"To determined the effects of regular medically prescribed and supervised exercise on multiple rehabilitative outcomes in male patients with healed MI" / Randomized clinical trial.	651 patients, 323 (Exercise) 328 (Control group) / 30 – 64 years / All men	Prescribed and supervised, long term exercise program	6 – 12 week intervention and 3 year follow up.	Non training group	Depression reduces with the mean difference of – 1.4 $\pm$ 3.7* at E2 level compared from E1 level of evaluation with a significant P value of 0.05. According to patients spouses, Katz adjustment measures, significant decrease of depression at E2 level. Mean difference - 0.7 $\pm$ 3.2* with significant P value of 0.05.	Moderate

Comments: The moderate level of evidence is due to some indirectness.
* Standard deviation

Appendix 8

Name of Author (Journal/Year/Vol)	Aim of Study/Study Design	Population (Sample/Age/Gender)	Intervention	Duration	Comparison group	Results	Grade of evidence
Oldridge *et al* (The American journal of cardiology / 1991 / 67)	"To determined the impact of a brief period of cardiac rehabilitation, initiated within 6 week of acute myocardial infarction (AMI)" / Randomized clinical trial.	177 (Rehabilitation = 87, Control group = 90) / 52.9 $\pm$ 9.5 (Rehabilitation), 52.7 $\pm$ 9.5 / 88% male (Rehabilitation group) and 89% male (Control group)	8 week intervention of exercise conditioning + cognitive behavioral group	8 week intervention and follow up for 4, 6, 8, 12 months.	Usual care	Decrease in depression was seen among intervention group and control group R (78), Control group (81) between the follow up (8 week, 4, 6,8,12 months) but not significant between time and among both groups. Baseline mean was 4.3 in rehabilitation group 3.4 (8 week), 2.4 (4 month), 2.5 (8 month), 2.7 (12 month). **Control group:** 3.9 at baseline, 3.6 (8 week), 3.1 (4 month), 2.8 (8 month), 2.7 (12 month).	Low

Comments: Low level of evidence is given due to exercise intervention combined with cognitive behavioral counseling which shows a important inconsistency and the result shows a lack of information leads to sparse data.

Appendix 9

Name of Author (Journal/Year/Vol)	Aim of Study/Study Design	Population (Sample/Age/Gender)	Intervention	Duration	Comparison Group	Results	Grade of evidence
Oldridge *et al* (Medicine and science in sports and exercise/ 1995/ 27)	"To examine the natural course of recovery, these observations require substantiation in studies with larger number of patients randomized to intervention or usual care" / Randomized clinical trail	187 patients, Intervention group = 94 (88% are male) and Control group = 94 (90% are male)/ Mean ± SD of age 54.3± 8.7 (Rehabilitation group) and 53.4± 9.4 (Control group)	Low level exercise with group behavior counseling to manage coping strategies (Individual counseling if necessary).	8 week intervention and 12 months follow up.	Control group receives usual care and desist from the intervention program but depends on the patients physicians to refer for cardiac rehabilitation.	Rehabilitation group shows significant improvement on decrease of depression from baseline 9.0 ± 9.6* to 6.6 ± 8.7* after 8 week of intervention with the p value of < 0.008‡ without comparing from control group. **12 months:** There significant change between 8 week baseline 4.2 ± 4.1* to 3.1 ± 3.7* in rehabilitation group only in time effect p value < 0.005‡ without treatment. But insignificant comparing from control group	Moderate

Comments: Moderate level of evidence is given due to exercise intervention combined with group behavior counseling which shows a important inconsistency.
* Standard deviation
‡ Significant

Appendix 10

Name of Author (Journal/Year/Vol)	Aim of Study/Study Design	Population (Sample/Age/Gender)	Intervention	Duration	Comparison Group	Results	Grade of evidence
Taylor *et al*(Journal of Psychosomatic Research / 1986 / 5)	"To determine the effects of exercise training programs on psychosocial improvement in uncomplicated post myocardial infarction patients" / Randomized controlled trial".	210 patients / 52 ± 9 years/ Male Home training: 70 Gym training: 67 Treadmill: 36 Control group: 37	Exercise training program divided into 4 categories: **1st category:** Treadmill testing with home exercise training **2nd category:** Treadmill testing with medically supervised gym exercise training. **3rd category:** treadmill testing without formal exercise training	3 – 26 weeks	**4th category**: "Controls where patients were seen only at 6 months for exercise testing after the MI".	Both the gym training group and home training group decreases the level of depression on both scales of depression but Significant changes were seen between the gym training group compared from no training group with the p value < 0.01 on both scales of depression (Hamilton and Beck depression scale) The mean score of Beck depression for gym training 2.9 at 3 week and 2.4 at 26 week where for no training 1.8 at 3 week and 2.0 at 26 week. Regarding Hamilton depression scale the mean of depression for gym training group at 3 week is 5.1 and 2.3 at 26 week as compare from no training group 3.5 at 3 week and 3.8 at 26 week.	Low
Comments: The low evidence was given due to the serious sparse data due to few observations and lack of information, some directness.							

Appendix 11

Excluded studies

Name of Author (Journal / Year / Volume)	Name of Study	Reason for exclusion
American heart journal / 2000 / 139	Enhancing recovery in coronary heart disease patients (ENRICHD): study design and methods. The ENRICHD investigators.	Psychosocial intervention
Beckie TM *et al* (International Journal of Nursing Studies / 2011 / 11)	The effects of tailored rehabilitation program on depressive symptoms in women: A randomized clinical trial.	Age ranges from 31 – 87 years
Beckie TM *et al* (Journal of Cardiopulmonary Rehabilitation and Prevention/ 2008/ 28)	Adverse baseline physiological and psychosocial profiles of women enrolled in a cardiac rehabilitation clinical trial.	Behavior change intervention
Blumenthal JA *et al* (Medicine and science in sports and exercise / 2004 / 36 (5))	Exercise, depression, and mortality after myocardial infarction in the ENRICHD trial.	Cognitive behavior therapy
Blumenthal JA *et al* (JAMA / 2005 / 293 (13))	Effects of exercise and stress management training on markers of cardiovascular risk in patients with ischemic heart	Quasi experimental design

	disease: A randomized controlled trail.	
Blumenthal JA *et al* (Journal of Cardiopulmonary Rehabilitation Prevention / 2010 / 30(2))	Enhancing standard cardiac rehabilitation with stress management training: Background, Methods, and Design for the ENHANCED study.	Stress management training intervention
Carinci F *et al* (European Heart Journal / 1997/ 18)	Role of interactions between psychological and clinical factors in determining 6-months mortality among patients with acute myocardial infarction.	Cohort study
Collins JA *et al* (Heart and Lung / 1997 / 26)	Effects of relaxation intervention in phase II cardiac rehabilitation: Replication and extension.	Quasi experimental study
Dala HM *et al* (International Journal of Cardiology/ 2007/ 119)	Home based versus hospital based rehabilitation after myocardial infarction: A randomized trial with preference arms-Cornwall Heart Attack Rehabilitation Management Study (CHARMS).	Aim is differ from our aim

Dixhoorn van J *et al* (European Journal of Cardiovascular Prevention and Rehabilitation/ 2005/12)	Relaxation therapy for rehabilitation and prevention in ischemic heart disease: A systematic review and meta-analysis.	Intervention of relaxation therapy
Grace SL *et al* (Journal of Womens Health/ 2008/ 17)	A prospective, controlled multi-site study of psychosocial and behavioral change following womens cardiac rehabilitation.	Quasi experimental design
Hevey D *et al* (Journal of cardiopulmonary rehabilitation / 2003 / 23 (1))	Four week multidisciplinary cardiac rehabilitation produces similar improvements in exercise capacity and quality of life to a 10 – week program.	Multifactorial rehabilitation program
Ickovics JR *et al* (Annals of Internal Medicine/ 1997/ 127)	Functional recovery after myocardial infarction in men: the independent effects of social class.	Beta block heat attack trial
Johansen S *et al* (Ugeskr Laeger / 2003 / 165 (34))	The effect of psychosocial rehabilitation after acute myocardial infarction. A randomized controlled trail.	Psychological intervention
Jolly K *et al* (Biomed central / 2003 / 3)	Home-based versus hospital-based cardiac rehabilitation after myocardial infarction or revisualization: design and rationale of the Birmingham Rehabilitation Uptake Maximization study (BRUM):	Primary aim based on cost effectiveness and effectiveness of home based rehabilitation compared from hospital-based cardiac rehabilitation.

	A Randomized controlled trail.	
Jolly K *et al* (International Journal of Cardiology/ 2006/ 111)	Home based cardiac rehabilitation compared with center based rehabilitation and usual care: A systematic review and meta-analysis.	Primary aim is different to our aim
Jolly K *et al* (BMJ Heart / 2009 / 95)	The Birmingham rehabilitation uptake maximization study (BRUM): A randomized controlled trial comparing home-based with center-based cardiac rehabilitation.	Age 61.8 $\pm$ 11.0
Jolly K *et al* (European Journal of Heart failure/ 2009/ 11)	A randomized trial of the addition of home based exercise to specialist heart failure nurse care: The Birmingham Rehabilitation uptake Maximization study for patients with congestive heart failure (BRUM-CHF) study.	Differ from our aim and objectives
Jones DA *et al* (BMJ / 1996 / 313)	Psychological rehabilitation after myocardial infarction: Multicenter randomized controlled trail.	Psychological intervention
Karonish IM *et al* (Journal of General Internal Medicine/ 2006/ 21)	Persistent depression affects adherence to secondary prevention behaviors after	Cohort study

	acute coronary syndromes.	
Kemenade TE *et al* (British Journal of Clinical Psychology/ 1994)	Effects of health education program with telephone follow up cardiac rehabilitation.	Counseling intervention
Kugler J *et al* (Archives of internal medicine rehabilitation / 1990 / 71)	Hospital supervised vs Home exercise in cardiac rehabilitation: Effect on aerobic fitness, anxiety, and depression.	Quasi experimental design
Lavie CJ *et al* (Mayo clinic proceeding / 1999 / 74 (10))	Effects of cardiac rehabilitation and exercise training program on coronary patients with high level of hostility.	Age 63 $\pm$ 11
Lavoie KL *et al* (American heart journal/ 2004/ 148)	Are exercise stress tests appropriate for assessing myocardial infarction in patients with major depressive disorder?	Different aim
Linden B *et al* (Intensive Critical Care Nursing /1995/ 11)	Evaluation of home-based rehabilitation program for patients recovering from acute myocardial infarction.	Comparative study design
Linden W *et al* (Achieves of Internal Medicine/ 1996/ 156)	Psychosocial interventions for patients with coronary artery disease: A meta-analysis.	Psychosocial intervention

Mayou RA *et al* (Journal of Psychosomatic Research / 2002/ 52)	Guideline – based early rehabilitation after myocardial infarction. A paragrmatic Randomized controlled trial.	Educational behavioral intervention
Mendes LCF *et al* (Journal of cardiopulmonary rehabilitation / 2006 /26 (1))	The effect of psychological intervention and quality of life after acute myocardial infarction: The enhancing recovery in coronary heart disease (ENRICHED) clinical trial.	Intervention based on Cognitive behavioral therapy
Michalsen A *et al* (Psychotherapy and Psychosomatics/ 2005/ 74)	Psychological and quality of life outcome from a comprehensive stress reduction and life style program in patients with coronary artery disease: results of a randomized trial.	Stress management intervention.
O'Neil A *et al* (Journal of Cardiopulmonary Rehabilitation Prevention/ 2011/ 31)	Impact of depression treatment on mental and physical health related quality of life cardiac patients: A meta-analysis.	Intervention of depression treatment
Parashar S *et al* (Archives of Internal Medicine/ 2006/ 166)	Time course of depression and outcome of myocardial infarction.	Different study design and aim
Rahe RH *et al* (Psychosomatic	Brief group therapy in	Brief group therapy, no

Medicine/ 1979/ 41)	myocardial infarction rehabilitation: Three to Four year follow up of a controlled trial.	exercise
Rees K *et al* (Cochrane/ 2009)	Psychological intervention for coronary heart disease (Review).	Physiological interventions
Roshanaei Moghaddam B *et al* (General Hospital Psychiatry / 2009/ 31)	The longitudinal effects of depression on physical activity.	Different aim
Scholz U *et al* (Socail Science and Medicine / 2006 / 62)	Physical activity and depressive symptoms in cardiac rehabilitation long-term effects of self-management intervention.	Age ranges from 31 – 86
Sebregts EHWJ *et al* (Journal of Psychosomatic Research/ 2008/ 58)	Psychological effects of a short behavior modification program in patients with acute myocardial infarction or coronary artery bypass grafting. A randomized controlled trial.	Stress management intervention
Serber ER *et al* (Journal of Cardiopulmonary Rehabilitation Prevention/ 2009/ 29)	Prevalence and characteristics of multiple psychiatric disorders in cardiac rehabilitation patients.	

Shen BJ *et al* (Journal of Behavioral Medicine/ 2004/ 27)	Independent and mediated contributions of personality, coping, social support and depressive symptoms to physical functioning outcome among patients in cardiac rehabilitation.	Psychosocial intervention
Silberman A *et al* (American Journal of Health Promotion/ 2010/ 24)	The effectiveness and efficacy of an intensive cardiac rehabilitation program in 24 sites.	Non experimental, Age
Trzcieniecka-Green A *et al* (European Heart Journal/ 1996/ 17)	The effects of stress management on the quality of life of patients following acute myocardial infarction or coronary bypass surgery.	Stress management intervention
Vizza J *et al* (Journal of cardiopulmonary Rehabilitation Prevention/ 2007/ 27)	Improvements in psychosocial functioning during an intensive cardiovascular lifestyle modification program.	Different aim and objectives
Wang W *et al* (Heart and Lung / 2012 / 14)	Effects of home based rehabilitation on health – related quality of life and psychological status in Chinese patients recovering from acute myocardial infarction.	Age ranges from 39 – 76 years

Yoshida T *et al* (Nursing and health Sciences / 1991 / 1)	Physical and psychological improvements after phase II cardiac rehabilitation in patients with myocardial infarction.	Aged 38 – 77
Zwister ADO *et al* (American Heart Journal/ 2007/155)	Hospital based comprehensive cardiac rehabilitation verses usual care among patients with congestive heart failure, ischemic heart disease, or high risk of ischemic heart disease: 12 month results of a randomized clinical trial.	Included heart failure, High risk patients also and don't know whether they are depressed before the intervention.

Appendix 12

AMSTAR criteria for systematic review and Meta-analysis studies

1. Was an 'a priori' design provided? The research question and inclusion criteria should be established before the conduct of the review.	☐ Yes ☐ No ☐ Can't answer ☐ Not applicable
2. Was there duplicate study selection and data extraction? There should be at least two independent data extractors and a consensus procedure for disagreements should be in place.	☐ Yes ☐ No ☐ Can't answer ☐ Not applicable
3. Was a comprehensive literature search performed? At least two electronic sources should be searched. The report must include years and databases used (e.g. Central, EMBASE, and MEDLINE). Key words and/or MESH terms must be stated and where feasible the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found.	☐ Yes ☐ No ☐ Can't answer ☐ Not applicable
4. Was the status of publication (i.e. grey literature) used as an inclusion criterion? The authors should state that they searched for reports regardless of their publication type. The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status, language etc.	☐ Yes ☐ No ☐ Can't answer ☐ Not applicable

5. Was a list of studies (included and excluded) provided? A list of included and excluded studies should be provided.	☐ Yes ☐ No ☐ Can't answer ☐ Not applicable
6. Were the characteristics of the included studies provided? In an aggregated form such as a table, data from the original studies should be provided on the participants, interventions and outcomes. The ranges of characteristics in all the studies analyzed e.g. age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported.	☐ Yes ☐ No ☐ Can't answer ☐ Not applicable
7. Was the scientific quality of the included studies assessed and documented? 'A priori' methods of assessment should be provided (e.g., for effectiveness studies if the author(s) chose to include only randomized, double-blind, placebo controlled studies, or allocation concealment as inclusion criteria); for other types of studies alternative items will be relevant.	☐ Yes ☐ No ☐ Can't answer ☐ Not applicable
8. Was the scientific quality of the included studies used appropriately in formulating conclusions? The results of the methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations.	☐ Yes ☐ No ☐ Can't answer ☐ Not applicable

9. Were the methods used to combine the findings of studies appropriate? For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e. Chi-squared test for homogeneity, I^2). If heterogeneity exists a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e. is it sensible to combine?).	□ Yes □ No □ Can't answer □ Not Applicable
10. Was the likelihood of publication bias assessed? An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test).	□ Yes □ No □ Can't answer □ Not applicable
11. Was the conflict of interest stated? Potential sources of support should be clearly acknowledged in both the systematic review and the included studies.	□ Yes □ No □ Can't answer □ Not applicable