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Pitout JDD, Church DL, Gregson DB, Chow BL, McCracken M, Mulvey M, Laupland KB (2007). Molecular epidemiology of CTXM-producing *Escherichia coli* in the Calgary Health Region: emergence of CTX-M-15-producing isolates. *Antimicrob. Agents Chemother.* 51: 1281-1286.

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Full Length Research Paper

Relationship between plasma levels of albumin, selenium, chromium and manganese of healthy subjects and patients with human immunodeficiency virus infection and acquired immune deficiency syndrome (HIV/AIDS), diabetes mellitus and cardiovascular disease in Akwa-Ibom and Cross River States of Nigeria

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Plasma albumin, selenium, chromium and manganese levels of thirty patients each with HIV/AIDS, diabetes mellitus and cardiovascular disease (CVD), and one hundred and six apparently healthy adults in Akwa-Ibom and Cross River States, South-South Nigeria was studied. The mean plasma albumin was higher in the control than in the disease patients. The mean plasma selenium was lowest in the control (0.004 ± 0.01 mg/L) than in the HIV/AIDS (0.007 ± 0.00 mg/L), diabetes mellitus (0.007 ± 0.00 mg/L) and CVD (0.010 ± 0.00 mg/L) patients. The mean plasma chromium was highest in the HIV/AIDS patients (0.125 ± 0.45 mg/L) and lowest in the diabetes mellitus patients (0.106 ± 0.04 mg/L). Plasma manganese level was highest in the control (0.028 ± 0.02 mg/L). Manganese was detected in the plasma of all the diseased patients. For the total healthy subjects, only 55.67, 68.87 and 83.93% had selenium, chromium and manganese detected in their blood plasma. There was no significant correlation between plasma levels of albumin, selenium, chromium and manganese ($P > 0.05$) in the control. The poor nutritional status of the disease patients was reflected by the depressed albumin levels.

Key words: Health, disease, trace elements, plasma levels.

INTRODUCTION

Many trace elements play important roles in a number of biological processes through their action as activators or

inhibition of enzymatic reactions by competing with other elements and proteins for binding sites, by influencing the

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permeability of cell membranes, or through other mechanisms (Al-Juboori et al., 2009). Trace elements such as zinc, selenium, chromium and manganese are important for maintaining a healthy immune system. Antioxidant nutrient deficiencies may hasten the progression of human immunodeficiency virus (HIV) disease by impairing antioxidant defenses (Stephensen et al., 2007), which influence the development of diabetes and its complications and cardiovascular disease (CVD) due to oxidative stress (Kangralkar et al., 2010; Sotiropoulos et al., 2011). Selenium as an essential mineral is required for the formation of selenoprotein enzymes which are vital for the immune system. Glutathione is the unique tripeptide essential for the functional physiology of the immune system. The raised glutathione levels make the immune system to go into anti-viral, anti-HIV mode and the T-cell function is enhanced (Zhao et al., 2000). Studies have shown that selenium could enhance insulin sensitivity by mediating insulin-like actions (Mueller and Pallauf, 2006) as selenium dependent enzymes are known to have antioxidant properties potentially protecting tissues and membranes from oxidative stress. Therefore, selenium is a co-factor of several key enzymes, the plasma levels of which determines the activities of glutathione peroxidase, thioredoxin reductase and deiodinase (Kohrle et al., 2005).

Manganese-activated enzymes play important roles in metabolism of carbohydrates, amino acids and cholesterol (Institute of Medicine, 2000). Increased levels of manganese can slow the activity of the reverse transcriptase enzymes, which HIV and other retroviruses use to convert their ribonucleic acid (RNA) to deoxyribonucleic acid (DNA) when they attack and infect human cells (Bolton et al., 2003). Manganese superoxide dismutase (MnSOD) is a principal antioxidant enzyme of mitochondria necessary for the proper development and growth of an organism (Aschner and Aschner, 2005). Manganese deficiency results in glucose intolerance similar to diabetes mellitus. In HIV patients, fasting insulin levels decrease with chromium supplementation. Chromium is a nutrient that potentiates the action of insulin, and may be an essential element for glucose metabolism (Stein et al., 2013). The ability of chromium to improve insulin sensitivity with apparently few serious side effects suggested a possible role for chromium supplementation in insulin resistance associated with HIV disease (Stein et al., 2013). Chromium is an essential element required for normal carbohydrate and lipid metabolism. Insufficient dietary chromium has been linked to maturity onset diabetes and cardiovascular disease. Chromium supplementation of subjects with elevated blood sugar following a glucose load leads to a decrease in blood sugar while hypoglycemics respond to supplemental chromium by an increase in hypoglycemic glucose values, increased insulin binding and alleviation of hypoglycemic symptoms (Kobla and Volpe, 2000).

Impaired glucose tolerance and type II diabetes result to adverse changes in lipid profiles and increased risk of cardiovascular diseases (Kobla and Volpe, 2000).

Plasma albumin is a useful indicator of the nutritional status of a population. A decrease in the serum concentration of albumin is associated with increased risk of death in patients with acute or chronic illness. Normal range of albumin concentration in human blood is 35 to 50 g/L (McPherson and Pincus, 2011). The aim of this study therefore was to compare the mean plasma levels of albumin, selenium, chromium and manganese in human immunodeficiency virus infection and acquired immune deficiency syndrome (HIV/AIDS), diabetes and cardiovascular disease patients, and in healthy individuals in Akwa-Ibom and Cross River states of Nigeria.

MATERIALS AND METHODS

One hundred and six apparently healthy subjects participated in this study and served as control. The population was made up of 40 men and 66 women. They were considered to be in good health based on medical histories and physical examination. The subjects were randomly selected from rural and urban communities of Akwa-Ibom and Cross States South - South Nigeria. All subjects ate ordinary foods available in their communities. Thirty patients with HIV/AIDS (15 men and 15 women), thirty patients with diabetes (15 men and 15 women) and thirty patients with cardiovascular diseases (19 men and 11 women) participated in the study. The patients were outpatients of the University of Calabar Teaching Hospital, Calabar, General Hospital, Ikom in Cross River State and St Luke's Hospital, Akwa-Ibom State.

Collection and preparation of samples

Blood was drawn in the morning into heparinised disposal plastic syringes with stainless disposal needles by peripheral venipuncture. Plasma was immediately separated out by centrifuging the blood samples at 3000 rpm for 10 min (Khalili et al., 2008). The samples were stored at -20°C until required for analysis (Akhlaghi et al., 2012).

Analytical method

Trace metals (selenium, chromium and manganese) were determined using a Unicam 939/959 Atomic Absorption Spectrophotometer as described by Kaneko (1999). Plasma albumin was determined by the bromocresol green method (Hill, 1985). Albumin in the sample reacted with bromocresol green in acid medium to form a coloured complex measured by spectrophotometry.

Statistical analysis

Statistical analysis of data was carried out using statistical package for the social sciences (SPSS) and the values expressed as mean \pm SD. Correlations between plasma levels of albumin, selenium, chromium and manganese in control and disease patients were determined using Pearson correlation. Significant difference was at $P \leq 0.05$.

Table 1. Mean plasma of albumin, selenium (Se), chromium (Cr) and manganese (Mn) in healthy subjects and disease patients.

Subjects	Trace elements			
	Albumin (g/L)	Se (mg/L)	Cr (mg/L)	Mn (mg/L)
Control	49.55±12.70	0.004±0.01	0.111±0.03	0.028±0.02
HIV/AIDS	28.42±8.75	0.007±0.00	0.125±0.45	0.003±0.00
DM	37.67±7.79	0.007±0.00	0.106±0.04	0.003±0.00
CVD	44.39±6.86	0.010±0.00	0.121±0.45	0.004±0.00

Table 2. Occurrence of trace elements in healthy subjects and disease patients.

Subjects	Number of subjects/Trace elements			
	Albumin	Se	Cr	Mn
Control	106	59	73	89
HIV/AIDS	30	10	16	30
DM	30	8	6	30
CVD	30	13	9	30

RESULTS

The mean plasma levels of albumin, selenium (Se), chromium (Cr) and manganese (Mn) in healthy subjects (control) and patients with HIV/AIDS, diabetes mellitus (DM) and cardiovascular diseases (CVD) are presented in Table 1.

The overall mean \pm SD plasma albumin concentration was (49.55±12.70 g/L) for 106 healthy subjects (control) with values higher than in the diseased patients. The HIV/AIDS patients had the lowest plasma albumin (28.42±8.75 g/L). The control had the lowest plasma selenium (0.004±0.01 mg/L) and highest plasma manganese (0.028±0.02 mg/L) concentrations than the diseased patients. Patients with CVD had the highest mean \pm SD plasma selenium and plasma manganese with mean \pm SD concentration of 0.010±0.00 mg/L and 0.004±0.00 mg/L respectively. The highest plasma chromium concentration was for HIV/AIDS patients (0.125±0.45 mg/L) and the diabetes patients had the lowest plasma chromium concentration of 0.106±0.04 mg/L. There was no significant correlation ($P>0.05$) between the plasma level of albumin, Se, Cr, and Mn levels within the control. Also, no significant correlation ($P>0.05$) was observed between the plasma albumin, Se, Cr, Mn of healthy subjects and patients of the three different diseases. But in the disease patients, there was inverse correlation ($r = - 0.434$, $P = 0.01$) between plasma albumin and manganese levels of HIV/AIDS patients, a negative correlation ($r = - 0.404$, $P = 0.05$) between plasma albumin and manganese of CVD and diabetes patients. There was an inverse correlation between plasma level of selenium and chromium ($r = - 0.447$) though not significant at $P > 0.05$. Table 2 shows

the occurrence of trace elements in the healthy subjects and disease patients. Manganese was detected in 89 healthy subjects out of the 106 subjects, and in the plasma of all the 30 HIV/AIDS, 30 diabetes mellitus and 30 CVD patients that participated in this study. Selenium was detected in 59 healthy subjects and only 10 HIV/AIDS, 8 Diabetes and 13 CVD patients. Chromium was detected in 73 healthy subjects and 16 HIV/AIDS patients, 6 diabetes patients and 9 CVD patients.

DISCUSSION

There is an increasing evidence for the important role which micronutrients play in the prevention of disease and promotion of overall health. Inadequate intake of a diet balanced in micronutrients however exists in Nigeria where there is widespread poverty (Kolawole, 2008). HIV infection is a major health problem in developing countries especially where malnutrition and nutritional deficiency prevail. HIV infected individuals are prone to malnutrition due to increased energy requirements, enteropathy and increased catabolism (Khalili et al., 2008). The low plasma albumin level observed in this study is an indication of deterioration in the state of health of the patients. The plasma albumin level in the HIV/AIDS patients was 42.6% lower than that of the healthy subjects which corroborates with the study of Khalili et al. (2008).

Malnutrition and HIV infection can deteriorate immune system function including decline in CD₄ lymphocyte count and delayed type immune reactions (Colecraft, 2008). The plasma level of selenium and chromium were slightly higher in the HIV/AIDS patients than in the control though there was no significant difference ($P > 0.05$). This was contrary to the studies of Khalili et al. (2008) and Akiibinu et al. (2012) who had lower plasma serum levels of Se in HIV/AIDS patients than in the control. HIV requires large amount of Se for its replication in the cells (Arinola and Akiibinu, 2005). The slightly higher plasma Se levels in this study could have been induced by use of antiretroviral therapy. Homeostatic mechanisms may initially operate or maintain or even increase the level of plasma Se. The specific role of Cr in HIV/AIDS infection remains largely undefined but interestingly, there is possibility that Cr increases lean body mass (Kobla and

Volpe, 2000). During most infections, the plasma levels of trace elements change but it is not clear if this reflects changes in the infected tissues. The very low levels of Mn in the HIV/AIDS patients observed in this study as compared to the control, though not significant, may be due to lack of activity of antioxidant enzymes (Akiibinu et al., 2012). Manganese is essential in the activity of antioxidant enzymes that protect the cells against highly toxic reactive oxygen species and also enhance the immunologic activities of phagocytes and lymphocytes (Akiibinu et al., 2012).

The plasma albumin level in the diabetes patients was 24% lower than that of the healthy patients. This could be due to the status of ill – health of the diabetes patients. The higher plasma Se levels in the diabetes patients corroborated with the study of Yang et al. (2011), who had serum selenoprotein concentrations significantly higher in patients with type 2 diabetes than normal patients. Selenoprotein and glutathione peroxidase are important for selenium storage and metabolism. Increasing evidence suggests that high selenium levels are associated with diabetes and CVD (Yang et al., 2011). Adewumi et al. (2007), revealed significantly lowered serum concentration of chromium and manganese in diabetic patients compared to the control. This is agreeable with the result of this study that showed lower plasma chromium and manganese levels. The very high plasma manganese level in the control than the diabetic patients disagreed with studies of Anetor et al. (2007) and Flores et al. (2011). Several dietary factors may affect manganese absorption for example dietary iron, presence of phytate and type of fat (Williams et al., 2010). Plasma manganese in this study for healthy Nigerians was generally high. There was a negative correlation between plasma albumin and manganese levels in the diabetic patients and this agreed with the study of Flores et al. (2011). Chromium is thought to play a key role in normal carbohydrate metabolism by potentiating the action of insulin leading to increase insulin sensitivity in type II diabetes and obesity (Sreekanth et al., 2008). This could be the reason for the lowered levels of chromium in the diabetic patients than healthy individuals in this study.

The plasma albumin was 10.4% lower in the cardiovascular patients than in the control. This could be due to the inadequate dietary intake of nutrients and also due to the infection. Plasma selenium and chromium were higher in the cardiovascular disease patients than in the control. Diet and nutrition have been extensively investigated as risk factors for major cardiovascular diseases like coronary heart disease and stroke, and are also linked to other cardiovascular risk factors like diabetes, high blood pressure and obesity (Reddy and Katan, 2004). Selenium deficiency has established implications in cardiovascular diseases particularly on cardiac muscle integrity (Safaralizadeh et al., 2005). This essential trace element takes part not only in the direct

protection of endothelial cells against the accumulation of aggressive oxygen species but also in biosynthesis of arachidonic acid derivatives involved in platelet and acid derivatives involved in platelet and leucocyte functions or in regulation of cholesterol (Kolaawole, 2008).

The values obtained in this study showed no significant correlation between plasma selenium levels in control and patients of cardiovascular diseases. This corroborated with the study of Stranges et al. (2006) that showed lack of significant association and effect of 200 g daily selenium supplementation with cardiovascular disease after 7.6 years follow up. Epidemiological studies assessing the role of chromium by Quallar et al. (2005) reported that higher levels of chromium were associated with lower risk of myocardial infarction in men. Supplementation with chromium picolinate, a stable and highly bioavailable form of chromium, has been shown to reduce the risk of CVD and type II diabetes (Hummel et al., 2007). The mean plasma chromium levels in this study for cardiovascular diseases patients were higher than control. The results do not indicate that plasma chromium levels in the patients reflect impairment of glucose tolerance. Mean plasma levels of manganese obtained in this study for cardiovascular disease patients were lower than the control. The low levels of plasma manganese in the cardiovascular disease patients could be due to the depressed activity of the antioxidant enzyme Manganese superoxide dismutase (MnSOD). Low activity of manganese superoxide dismutase could cause an increase in the level of superoxide radicals and thus increased oxidative stress (Zablocka et al., 2012.)

The plasma levels of selenium, chromium and manganese of healthy subjects showed detection of only 55.67, 68.87 and 83.96% respectively of the trace elements. Adequate intake (AI) of selenium is 55 µg/day for women and 70 µg/day for men (FNB, 2001). Studies in Nigeria showed mean plasma selenium to be 0.188±0.026 mg/L (Babalola et al., 2003) and 0.057±2.50 mg/L (Arinola and Charles – Davis, 2008). The AI of chromium 35 µg/ day for men and 25 µg/L for women (FNB, 2001) while the plasma chromium is between 0.18 and 0.47 mg/L or less than 0.50 mg/L (Chernecky and Berger, 1997). The AI for manganese is 2.3 mg/day for men and 1.8 mg/L for women while blood serum manganese is between 0.003 to 0.010 mg/L for healthy adults (FNB, 2001). The low plasma selenium as shown by the values obtained could be as a result of foods and diets consumed by the participants of this study which were made up of starchy foods, cereals and fruits. Selenium has been shown to be more available from diets of animal origin than those of plant sources (Combs, 2001).

CONCLUSION

The plasma levels of manganese and chromium in the healthy adults seemed adequate but the plasma selenium

seemed to be low when compared with values obtained in other studies. The HIV/AIDS, diabetes and cardiovascular disease patients had lower plasma albumin which was an indication of deteriorating health. People with poorly controlled diseases are susceptible to multiple micronutrient deficiencies. They should be educated on the importance of acquiring these nutrients from natural food sources in order to reduce high risk of diseases.

Conflict of interest

The authors declared that they have no conflict of interest.

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Full Length Research Paper

Assessing healthy diet affordability in a cohort with major depressive disorders

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Although, the cost of food is commonly described as a barrier to consuming a healthy diet, the evidence for this viewpoint has been inconsistent to date. The purpose of this study was to assess whether a healthy diet is affordable for a sample population with major depressive disorder and current unhealthy eating patterns, enrolled in supporting the modification of lifestyle in lowered emotional states (SMILES) trial. The first 20 participants of the SMILES trial were invited to complete a 7-day food diary at baseline. A cost analysis of a modified Mediterranean diet (recommended for trial participants) and 7-day food diaries of participants enrolled in the randomized controlled trial was conducted. Trial participants spent an estimated mean of \$138 per week on food and beverages for personal consumption, whereas the total food and beverage costs per person per week for the recommended modified Mediterranean diet was estimated at \$112, both based on mid-range product cost. The modified Mediterranean diet at \$1.54 per mega-joules (MJ) was cheaper per energy unit than the cost of the current dietary intake of the SMILES participants included in this study at a mean of \$2.35 per MJ. These study findings suggest that the adoption of a healthy modified Mediterranean diet does not cost more than a poor quality diet. Thus, failure to comply with healthy diets is unlikely to reflect affordability. Public health messages should incorporate the finding that healthy eating is not associated with increased costs and in fact may well involve savings to the household budget. Practical strategies and techniques for selecting healthy nutritious foods on a budget could support the achievement of desired dietary goals for preventing and managing chronic disease.

Key words: Depression, cost analysis, food cost, healthy diet, Mediterranean diet.

INTRODUCTION

Chronic diseases, such as coronary heart disease, stroke, type 2 diabetes and depression, are the leading causes of death and disability worldwide (World Health Organization (WHO, 2014a,b); representing 63% of all

deaths (WHO, 2014). Nutrition is a major modifiable determinant of chronic disease, with scientific evidence increasingly supporting the view that diets (healthy or poor) have profound effects on health throughout life

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(Joint WHO/FAO Expert Consultation on Diet, 2002). Importantly, diet quality may influence not only present health, but may predict whether or not an individual will develop certain chronic diseases later in life (Joint WHO/FAO Expert Consultation on Diet, 2002). This is also pertinent in the context of mental health, where healthy diet has recently been identified as a protective factor in depressive illness (Lai et al., 2013). Depression is highly prevalent and a leading cause of disability globally (Psaltopoulou et al., 2013).

In recognition of this established evidence-base, advice to adopt a 'healthy diet' is included in clinical practice guidelines for the management of overweight and obesity (Dietitians Association of Australia (DAA), 2005), type 2 diabetes mellitus (Ajala et al., 2013; Dietitians Association of Australia (DAA), 2006) and stroke (National Stroke Foundation, 2010). However, despite the degree of evidence available, adherence to dietary advice is typically poor (Ball et al., 2003). One of the proposed reasons is the perception that healthy food is more expensive than unhealthy food (Goulet et al., 2008; Ryden et al., 2008; Turrell and Kavanagh, 2005; Vlismas et al., 2010). For persons from socioeconomically disadvantaged backgrounds, who already allocate a higher proportion of their disposable income to food (Drewnowski and Specter, 2004; Palermo et al., 2008), cost is argued to be of particular importance given the higher prevalence of chronic disease in those with low socioeconomic status (Joint WHO/FAO Expert Consultation on Diet) (Glover et al., 2004; Rao et al., 2013; Vlismas et al., 2010). Although, the cost of food is commonly described as a barrier to consuming a healthy diet (Kettings et al., 2009; Lopez et al., 2009; Rao et al., 2013; Ryden et al., 2008; Turrell et al., 2005) the evidence for this viewpoint has been inconsistent to date. Some studies have found that a healthy diet is associated with increased costs (Bernstein et al., 2010; Lopez et al., 2009; Rao et al., 2013) while others have reported that it is not more expensive to eat healthily (Goulet et al., 2008; Ryden et al., 2008).

It is likely that the literature to date lacks clarity because of varying methods employed, not all of which are designed to answer the question; "are food costs a barrier to healthy eating"? Specifically, studies do not accurately measure current dietary intake and the associated expenditure at an individual level, based on analysis of a poor quality and better quality diet scenario. Additionally, studies differ with regards to methods of dietary assessment, the definition of what constitutes a 'healthy diet' and the approach to costing the diet.

Dietary assessment

Some studies compare the cost of individual food items rather than whole diets (overall diet patterns), for example lean cuts of meat versus high fat sausages. Descriptions of a healthy diet can also vary and have

been defined by adherence to a Mediterranean style diet (Lopez et al., 2009) or scores on the Healthy Eating Index (Bernstein et al., 2010) while other studies define diet quality based on the intake of select macro- and micronutrients (Aggarwal et al., 2011). This heterogeneity in what characterises a healthy diet poses a number of challenges when interpreting and comparing results. Moreover, studies that use participant reported eating patterns as the basis of analyses may introduce further uncertainty, as common dietary assessment tools fail to gather information of sufficient detail to determine true dietary intake. For example, the commonly employed food frequency questionnaires (FFQs) are limited by the food lists they contain, and attempt to assess usual intake over prolonged periods and across different seasons. FFQs typically lack specific detail regarding serving sizes, such that this information is often based on standardised portion sizes of specific foods published in National dietary guidelines (Vlismas et al., 2010), which does not account for individual variation (Rangan et al., 2009). Other studies use self-reported 24 h recall (Aaron et al., 2013) or dietary histories in a face-to-face interview (Turrell and Kavanagh, 2005), which are prone to recall bias and poor reliability at the individual level (Thomas B, 2002). Few studies use 7-day diet records (Rao et al., 2013), commonly referred to as the 'gold standard' dietary assessment tool (Hoidrup et al., 2002).

Assessing food costs

The methods for estimating food costs in published studies tend to be described in only general terms, for example using national food prices or a food purchasing index (example, food-cost data from the US Department of Agriculture or a purchasing index based on 16 grocery items) (Bernstein et al., 2010; Turrell and Kavanagh, 2005). Such methods are faced with limitations given the wide diversity in food prices for designated food items which vary with packing size (bulk purchasing), branding, type of outlet, season etc. Furthermore, measures of affordability are commonly based on National data of disposable income or average household spending (example, the proportion of household income required to be spent on healthy food) (Palermo et al., 2008; Vlismas et al., 2010; Ward et al., 2012; Wong et al., 2011). Thus, these studies fail to accurately examine food affordability from the consumers' perspective.

This study seeks to address a number of these methodological limitations. Our aim was to assess whether a healthy diet is affordable for a sample population with major depressive disorder (MDD) and current unhealthy eating patterns. The research tasks were to:

1. Calculate the cost of the current poor quality diets consumed by a sample of individuals with MDD enrolled

in the Supporting the Modification of lifestyle in Lowered Emotional States (SMILES) trial (O'Neil et al., 2013).

2. Estimate the cost of an alternative healthy Modified Mediterranean diet recommended for trial participants and

3. Compare the cost of the current poor quality diet with the healthy modified Mediterranean diet to assess affordability.

To our knowledge this is the first published cost analysis of foods consumed by individuals with MDD based on the gold standard 7-day food diary. It is also the first study to explore, for a sample of persons with a major chronic disease and poor diet quality, whether food cost is a plausible explanation for poor food choices, based on costs of their current diet pattern and the cost of an alternative healthy diet. These study findings are likely to be generalizable to other population groups considering that almost half (45%) of all Australians will experience a mental disorder at some point in their lifetime (Australian Bureau of Statistics (ABS), 2009). Moreover, the poor quality diets consumed by study participants are likely reflective of dietary habits of the general Australian population - most of whom fail to meet National Dietary Guidelines (Australian Bureau of Statistics (ABS), 2010).

METHODOLOGY

Subjects and dietary assessment

Participants comprised individuals enrolled in a randomized, controlled trial of dietary improvement as a treatment strategy in major depression, the SMILES study (O'Neil et al., 2013). Because 7-day food diaries were collected as part of this RCT, it provided a unique opportunity to assess the cost of current poor quality diets in a chronic disease cohort, and whether food cost was an issue in promoting better food choices. Participants were recruited across two intervention sites, Geelong and Melbourne (Victoria, Australia). Eligibility criteria required study participants to currently have "poor" dietary quality assessed using a dietary screening tool (DST) (Bailey et al., 2009), modified for the Australian population. Participants with a score of 68 or less on the DST were eligible for inclusion (O'Neil et al., 2013).

Broadly defined, these individuals had a poor (low) intake of dietary fibre, lean proteins, and fruit and vegetables, and a high intake of sweets, processed meats and salty snacks (Bailey et al., 2009). Depression status was assessed using the Diagnostic and Statistical Manual of Mental Disorders 4 (DSM-IV-TR) diagnostic criteria for major depressive disorder, single episode or recurrent. Depression severity was assessed using the Montgomery-Asberg Depression Rating Scale (MADRS); participants required a score of 18 or above (moderate to severe depression) to be eligible. Further details have been published previously (O'Neil et al., 2013).

The first 20 participants to complete a 7-day food diary (Garrow et al., 2002) at the baseline assessment (before randomization and group allocation), conducted between November, 2012 and April, 2013, were included in this study. Food diaries were self-reported written records of actual intake of foods and beverages. Participants were encouraged to record their intake at the time of consumption to minimise error. At the baseline assessment, with the participant present, a research assistant (RA) examined the completed food diaries in detail to check for missing data or potential errors. Portion sizes were checked using food models and

household measures. In situations where portion size information could not be accurately obtained from the participant (example, poor recall) a number of reputable published resources were utilised to assign a 'typical' portion size (Borushek, 2012; National Health and Medical Research Council (NHMRC), 2013; Rangan et al., 2009; Xyris Software (Australia) Pty Ltd, 2012). Food diaries were analysed using AUSNUT 2007 database in Foodworks 7.0.8923 (Xyris Software (Australia) Pty Ltd, 2012) to determine average daily energy intake, expressed as MJ.

Weight and height measurements (using a stadiometer) were collected by a RA to allow for calculation of body mass index (BMI) (kg/m^2). BMI was used to calculate estimated energy requirements (EER) to assess likely accuracy of dietary reporting. Under and over-reporting were measured using the Goldberg cut-off method (Black, 2000) to provide an indicator of the likely validity of the food diary information. Under and over reporting was based on the relationship between energy intake (EI) and EER. EI was calculated based on reported intake from 7-day food diaries, and the Schofield equations (Stewart, 2009) were used to calculate EER. Under-reporters were defined as $\text{EI}:\text{EER} < 0.76$, acceptable reporter defined as $\text{EI}:\text{EER} 0.76$ to 1.24 , over-reporter defined as $\text{EI}:\text{EER} > 1.24$ (Black, 2000). Under and over-reporters were not excluded from the analysis but their impact on findings was explored.

Healthy alternative - modified Mediterranean diet

To assess healthy diet affordability, the food costs of the current poor quality diets consumed by study participants at baseline were compared to the modified Mediterranean diet recommended to individuals enrolled in the SMILES trial. The modified Mediterranean diet, developed specifically for the SMILES trial, includes recommended serves of each of the following food groups: to achieve the macronutrient profile detailed in Table 1:

1. Non-refined cereals
2. Vegetables
3. Pulses (example, lentils and chickpeas)
4. Nuts
5. Fruit
6. Red meat, chicken, eggs and fish
7. Dairy
8. Olive oil
9. Wine
10. Sweets

Further details have been published previously (O'Neil et al., 2013).

COSTING METHODOLOGIES

Overview

Three research assistants (RAs) (LN, SD, JP) and one accredited practicing dietitian (RSO) completed the cost analyses of the modified Mediterranean diet and of the 7-day food diaries, reflecting advice on the costing method by a health economist Leonie Segal (LS). Costing of the modified Mediterranean diet occurred between January and February, 2013, and the food diaries were costed between April and July, 2013.

Participant diets at baseline (poor quality diet)

Using the 7-day food diaries, a purchase cost was applied to every food and fluid item recorded in the diaries. Total estimated weekly cost of the participant's diet was simply equal to the sum of the daily costs for all seven days (\$ / week). Current dietary patterns and their associated costs were taken as the best indicator of the available food budget.

Table 1. Nutrient profile of the modified Mediterranean diet.

Nutrient profile	Average/Day	Percentage of energy contribution
Energy	9.9 MJ*	-
Protein	104.3 g	18
Total fat	103.6 g	39
Saturated fat	23.3 g	9
Monounsaturated fat	53.6 g	20
Polyunsaturated fat	19.7 g	7
Carbohydrate	220.5 g	37

*Energy with alcohol (110 ml red wine /day @ 450 kJ) = 10.4 MJ.

Modified Mediterranean diet (healthy diet)

The total cost of the modified Mediterranean diet was calculated by assigning a price (medium, low, high) to each food item. These costs were then multiplied by the weekly consumption frequency of servings of that food group. Total cost of the diet was equal to the sum of all food types in \$ / week. The healthy diet cost analysis was based on a modelled meal plan, and we did not conduct a diet cost comparison based on actual diet patterns or actual food purchases. Finally, the total weekly cost of the modified Mediterranean diet was compared to the total cost of the participant's 7-day food diaries.

Participant food diaries

The woolworths on-line website (www2.woolworthsonline.com.au) was used to establish participant food expenditure. Woolworths is one of two largest supermarket chains in Australia, which are competitively (similarly) priced and together account for roughly 80% of all grocery sales (National Association of Retail Grocers of Australia (NARGA), 2010). The site was accessed between April, 2013 and July, 2013. Where a participant reported consuming a specific brand or product (example, Kellogg's Nutri-Grain or Rev milk) the quoted price for that product was used. Otherwise a medium cost product was selected, which was crosschecked by two RAs. For each food item such as 'white bread' or 'canned tuna' all items in that category were identified and a product in the mid-price range was selected. This process was independently conducted by LN, SD, JP, RSO and any discrepancies resolved in discussion with RSO. The mid-cost item was commonly priced at 30 to 60% above the low cost item and 20 to 50% below the high cost item. Where seasonal fruits consumed were no longer available at time of costing (example, berries, cherries and mangoes) current data on the average price of fruit was obtained (Department of Primary Industries et al., 2014). The Victorian Healthy Food Basket (Palermo and Wilson, 2007) was used to guide the selection of product volumes/pack size. For products with a short shelf life (example, eggs and milk) smaller purchase volumes were used. Whereas, products with a longer shelf life (example, olive oil and rice) larger purchase volumes were used. Otherwise a mid-range product volume/pack size was assumed to be purchased. A sensitivity analysis was conducted around the food cost estimate. In all scenarios, the same pricing assumption (low, medium or high) was applied to both the poor quality and healthy diet.

Mixed meals

A mixed meal is a meal comprising a variety of food groups example, lasagne or stir-fry. Mixed meals prepared at home were broken down into their individual components and costed as per

methods above. Additionally, if the location of meal consumption was not specified, it was assumed to have been prepared at home. Mixed meals specified as purchased outside of the home were costed using the menu price list from the specified eating venue. If the eating venue was not specified Urbanspoon (www.urbanspoon.com) was used to identify cafés or restaurants located in Collingwood or Melbourne (the main intervention site). Restaurants of the specified cuisine with a \$ (cheap eats) symbol were selected or moderately priced restaurants (\$\$ symbol) were chosen if 'cheap eats' restaurants lacked the relevant information. Menus needed to be available on-line.

Missing data

If any days were incomplete, a food cost was entered based on the average cost of the other recorded days. When foods did not incur a direct cost to the participant (example, food supplied at a work function or party), an average meal value was allocated based on the respective participant's food diary.

Healthy alternative - Modified Mediterranean diet

Product selection and data sources

As described earlier, Woolworths online (www2.woolworthsonline.com.au) was used to ascertain cost of food items. If a product was not available on this website, Coles on-line (<http://shop.coles.com.au>) was utilised. As previously noted medium priced items were selected for the primary analysis. Sale prices were not used. Low and high cost items were also recorded to generate a high and low cost alternative in sensitivity analysis. A wide range of information was gathered to account for the variation in food costs due to factors such as branding, whether fresh or frozen, organic or mass produced, product size (whether purchased in bulk) and outlet type (example, supermarket or local store). Similar product volumes / pack size were selected across the three cost categories in an effort to limit further cost variation associated with bulk purchases.

Food cost per person per week

Once purchase costs were established, these figures were converted to a cost per person per week based on the daily / weekly consumption frequency of servings of that food group. Portion sizes (and frequency of servings) were based on the modified Mediterranean diet guidelines (O'Neil et al., 2013). The mid-point was used where a range in portion sizes were specified (for example; 65 to 100 g cooked meat was converted to 82.5 g per day).

Table 2. Example of costing calculations for modified Mediterranean diet.

Food item	Purchase cost			Daily intake	Intake per week	Cost per week		
	High	Medium	Low			High	Medium	Low
Bread, wholegrain	Burgen (700 g, 1 loaf) \$5.29	Mighty soft (700 g, loaf) \$3.19	Homebrand (650 g, 1 loaf) \$1.50	2 slices (50 g)	14 slices (350 g)	Burgen \$2.64	Mighty soft \$1.59	Homebrand \$0.81
Red meat	Beef Steak, Porterhouse (1kg) \$24.07	Lamb, midloin chops (1kg) \$16.99	Beef Mince (1kg) \$7.96	1 serve ≡ 82.5 g	3 to 4 serves ≡ 248 – 330 g	Beef steak, Porterhouse \$5.97 – 7.94	Lamb, midloin chops \$4.21 – 5.61	Beef Mince \$1.97 – 2.63

Table 2 shows an example of the costing calculations.

Sensitivity analysis

For the sensitivity analysis an assumption was made that participant spending patterns and behaviours would not change when substituting unhealthy foods for healthy foods. For example individuals who habitually purchase home-brand products would continue to purchase these generic products. Thus, the sensitivity analysis compared low cost products of trial participants with low cost products of the modified Mediterranean diet, and high cost products of trial participants with high cost products of the modified Mediterranean diet. The sensitivity analysis was limited to varying unit food costs; as the parameter subject to greatest uncertainty. A low and high cost alternative was specified to selected food groups; taken as – and + 33% of the middle value and applied to both the poor quality and modified Mediterranean diet. A small number of food items for which prices have little variability such as milk were not adjusted. As only 45% (9/20) of study participants consumed alcohol according to the 7-day food diaries, an adjusted figure was applied to the modified Mediterranean diet to reflect an average alcohol intake across the group (45% of \$15.19).

Cost per energy unit (\$ / MJ)

Due to potential differences in EI (according to 7-day food diaries), and the energy contribution of the modified Mediterranean diet, there was a need to adjust the dietary

intake and cost to equivalent energy levels. The daily cost per energy unit (\$ / MJ) for: the 7-day food diaries was equal to the daily food expenditure (\$) divided by average daily EI for each participant; the modified Mediterranean diet was equal to the average daily food costs (\$) divided by the total energy contribution (10.4MJ) for medium cost products.

RESULTS

Sample characteristics

Characteristics at baseline of adults enrolled in the SMILES trial are displayed in Table 3. The sample was 65% female, 35% of participants were overweight (BMI ≥ 25 kg/m² <30 kg/m²) and 45% obese (BMI ≥ 30 kg/m²). Using the MADRS as a measure of depression status, 80% of participants had moderate depression and 20% had severe depression. Ninety percent of the participants had completed at least secondary school. Compared to Australian population figures, 70% of 25 to 64 year olds have at least upper secondary education (Australian Bureau of Statistics (ABS), 2010b). With regards to diet quality, scores on the DST ranged from 26 to 61. All participant diets were well below the eligibility cut off score for a poor quality diet of 68 or less.

Participant 7 day food diary costs

All 20 participants completed a food diary. There were seven missing days across the group which was mainly attributed to one participant recording their intake for four days only. Based on the 7-day food diaries and costing method described above, participants spent a mean \$138 per week on food and beverages for personal consumption (Table 4). Expenditure varied widely from \$53 to \$239 per week. Yet, expenditure was evenly distributed across the range, with the median at \$130, only slightly below the mean. The mean cost per megajoule was \$2.35 (R:1.20 to 4.59). The calculations are available on request to the lead author. Participants spent on average almost one third (32.7%) of their total food expenditure on extras for example, alcohol, deep fried food and chocolate (see supplementary material with *extras* defined). Only four individuals (20%) spent less than 25% of their total food expenditure on extras. These four participants purchased meals outside the home as frequently as the other participants, however the meals selected were more nutritious, and were thus not classified (or costed) as an extra for example, Asian stir-fry or vegetarian curry.

Table 3. Characteristics at baseline of adults enrolled in the SMILES trial.

Characteristic		Total N = 20
Age (years)	Mean±SD	40.25±11.35
	Range	22 to 63
Gender	Male, n (%)	7 (35%)
Weight (kg)	Mean±SD	85.06±18.35
	Range	64.0 to 136.7
Body Mass Index	Mean ± SD	29.11±5.10
	Range	21 to 41
BMI		
Obese (≥30 kg/m ²)	N (%)	9 (45%)
Overweight (≥25 kg/m ² <30 kg/m ²)	-	7 (35%)
Healthy weight (<25 kg/m ²)	-	4 (20%)
MADRS		
Moderate (≥18 and < 31)	Mean±SD	25.45±5.36
Severe (≥31) Müller et al. (2003)	Range	19 to 37
	N (%)	16 (80%), 4 (20%)
DST	Mean±SD	49.55±10.6
	Range	26 to 61
Highest educational attainment; n (%)	Primary school	2 (10)
	Secondary School	5 (25)
	Apprenticeship/trade	3 (15)
	Bachelor degree	6 (30)
	Postgraduate degree/certificate	4 (20)
	Doctoral degree	0 (0)
Living arrangement; n (%)	Single	9 (45)
	Married / de facto	7 (35)
	Living with friends or family	4 (20)
	Widow/widower	0 (0)
Children; n (%)	Yes	9 (45)

SD = standard deviation, BMI= Body mass index.

Modified Mediterranean diet costs

The total food costs per person per week for the modified Mediterranean diet was estimated at \$105 (excluding red wine) or \$120 including red wine, based on mid-range product cost. Based on adjusted alcohol intake, the total food cost per person per week for the modified Mediterranean diet was estimated at \$112. The highest share of food cost was for vegetables (22.5%) followed by dairy (15.7%), fruit (14%) and meat (14%) (Table 5). The mean cost per MJ was \$1.54. The modified Mediterranean diet classified extras as red wine, dark chocolate, lollies and dairy dessert. At the medium cost bracket, extras contributed 14.4% of the total food expenditure.

Comparing cost of 7-day food diaries to modified Mediterranean diet

Total cost

The mean food expenditure of SMILES participants at \$138 per week was higher than the estimated cost of the modified Mediterranean diet of \$112 per person per week with both cost estimates based on medium product prices. For 60% of participants, their current estimated weekly expenditure on food was at least equal to (or greater than) the cost of the recommended Mediterranean diet. This compares to the average household expenditure of \$204 (Australian Bureau of Statistics (ABS, 2011) per week for food and non-

Table 4. Participant expenditure, cost per MJ and cost of extras as a percentage of total expenditure (April – July 2013 prices).

Participant #	Average daily expenditure (total diary days completed) (\$)	7-day expenditure (\$)	Cost per MJ (\$)	Cost of extras as a percentage of total expenditure (%)
1	11.25 (6)	78.73	1.92	34.21
2	16.72 (7)	117.02	1.43	31.03
3	27.25 (9)	190.73	3.50	39.83
4	15.12 (6)	105.82	1.98	31.08
5	33.69 (6)	235.80	3.62	36.77
6	32.00 (7)	224.02	4.59	33.61
7	22.67 (6)	158.71	2.83	22.49
8	7.59 (7)	53.16	1.66	47.52
9	24.43 (7)	170.98	3.66	8.25
10	17.38 (7)	121.69	1.55	41.24
11	19.82 (7)	138.77	2.41	35.27
12	20.49 (7)	143.40	2.41	33.40
13	12.30 (4)	86.07	1.52	27.82
14	14.23 (7)	99.62	1.74	32.41
15	12.32 (7)	86.26	1.59	51.98
16	11.40 (7)	79.81	1.20	7.44
17	25.53 (7)	178.70	2.39	35.25
18	10.75 (7)	75.25	1.40	44.33
19	34.22 (7)	239.57	3.21	20.08
20	25.67 (7)	179.68	2.36	39.73
Mean (\pm SD)	\$19.74 (\pm 8.14)	\$138.19 (\pm 56.95)	\$2.35 (\pm 0.94)	32.69% (\pm 11.38)
Range	\$7.59 – 34.22	\$53.16 – 239.57	\$1.20 – 4.59	7.44 – 51.98%

alcoholic beverages in Australia in 2009 to 2010, or an estimated \$215 in 2012 (adjusting for the food price component of the Consumer Price Index (Australian Bureau of Statistics (ABS), 2014). With a mean household size of 2.6 persons (Australian Bureau of Statistics (ABS), 2010a), this suggests a food cost per adult of \$107.50 per week (adjusting for lower food costs for children).

Energy intake and cost per energy unit

To allow for further comparisons of weekly food costs for participants with current poor quality diets and weekly costs of the modified Mediterranean diet the cost data above was adjusted to account for over and under-reporting as well as differences in energy contribution of the diets. According to the 7-day food diaries, participants consumed 4.58 to 11.71MJ per day, however, one quarter of participants were considered under ($n = 4$) or over reporters ($n = 1$) using the Goldberg cut-off (Black, 2000). Five participants had EER's that exceeded the energy contribution of 10.4 MJ of the modified Mediterranean diet. For these participants, relative to EERs the modified Mediterranean diet was

inadequate in energy by 0.21 to 2.31MJ. The modified Mediterranean diet at \$1.54 per MJ was cheaper per energy unit than the cost of the current dietary intake of SMILES participants at a mean \$2.35 per MJ, with both diets costing at medium priced product options.

Spending patterns

For medium cost products of the modified Mediterranean diet, extras made up 14% of the total food expenditure. In comparison, all but two SMILES participants spent 20% or more of their total food costs on extras with the mean extras spending just over double (32%) of the Modified Mediterranean diet.

Sensitivity analysis

Sensitivity analysis modified Mediterranean diet

The total low and high cost food estimates per person per week for the modified Mediterranean diet were \$75 and \$150 per week, respectively. There was a large cost

Table 5. Modified Mediterranean diet -Total food costs for each food group (weekly intake).

Food group	High (\$)	Medium (\$)	Low (\$)	Cost difference percentage (medium to high)	Cost difference (medium to low)
Cereals	12.99	8.67	5.50	49.8	57.6
Vegetables	38.74	27.03	14.15	43.3	91.0
Nuts	7.80	6.96	5.15	12.1	35.1
Pulses	2.68	1.35	0.67	98.5	101.5
Fruit	23.09	16.83	11.35	37.2	48.3
Meat, chicken, eggs, fish	22.65	16.91	10.20	33.9	65.8
Dairy	26.30	18.78	13.94	40.0	34.7
Olive oil	7.49	6.31	5.22	18.7	20.9
Sweets	2.17	2.07	1.49	4.8	38.9
Total (\$) (without red wine)	143.90	104.91	67.67	-	-
Total (\$) (including red wine*)	159.10	120.10	82.86	-	-
Total (\$) (including adjusted red wine intake**)	150.74	111.75	74.51	-	-

*Cost for red wine of \$15.19 was based on average consumption in 2007 (Ross et al., 2010).** Adjusted red wine intake (45% of \$15.19) = \$6.84

^Cost per energy unit = \$1.54 (average daily consumption of \$15.96 divided by 10.4 MJ).

variation between high and low cost products; percentage differences ranged from 43.5 to 301.8%, relative to low cost products. Food costs were affected by many factors including branding, freshness, seasonality, cuts of meat and whether or not the product was organic. For example; home brand products were less expensive than their branded counterparts, frozen or tinned vegetables and fish were cheaper than fresh options, selecting fruit and vegetables in season was more cost effective and beef mince was less expensive than porterhouse steak.

Sensitivity analysis participant 7-day food diaries

The values for the sensitivity analysis of participant food diaries was driven by the cost estimates from the modified Mediterranean diet where a low and high cost alternative was taken as – and + 33% of the middle value. Thus, mean spending for trial participants increased to \$183 per person per week for high cost products and reduced to \$92 for low cost products.

Sensitivity analysis comparing modified Mediterranean diet to participant food diaries

When comparing the low cost products of the modified Mediterranean diet to the low cost products of the poor quality diet the modified Mediterranean diet was found to be considerably cheaper; \$75 versus \$92, respectively. Additionally, the modified Mediterranean diet was substantially cheaper than the poor quality diet when high cost products were costed; \$150 versus \$183, respectively.

DISCUSSION

The results of this cost analysis suggest that a healthy

Mediterranean-style diet can be affordable for individuals with MDD whose habitual diet is of a poor quality. These findings suggest that individuals are adopting poor quality diets for reasons other than food costs. For this population with MDD, it is pertinent that emotional distress and especially symptoms such as depression and fatigue are known to generate cravings for sugary or high fat foods, such as ice-cream, chocolate bars and fast-food. Consumption of these foods, results in a temporary mood improvement, but eventually the negative mood state returns and the cycle starts again (Christensen and Brooks, 2006; Meyer et al., 2013; Mikolajczyk et al., 2009; Oliver and Wardle, 1999). Furthermore, depressive symptoms may decrease an individual's motivation to engage in healthy dietary habits, and thus may lead to poor dietary choices (Anton and Miller, 2005). Consistent with these theories, the mean spending on “extras” by SMILES participants was just over double that of the modified Mediterranean diet. Common extras amongst trial participants included deep-fried food, pastries and chips; cakes, chocolate and sweet biscuits; alcohol; soft drink and meals eaten outside the home example, pizza and fast-food items.

Results of this study also suggest that individuals could achieve a healthy diet at even lower cost than our mid-priced scenario, by purchasing cheaper product items from the Mediterranean diet such as pulses, canned fish, frozen or tinned vegetables and purchasing less alcohol, soft drinks, sweets and meals eaten outside the home. Other strategies that could be employed to achieve a nutritionally balanced diet at lower cost include; selecting home brand products rather than branded counterparts; purchasing fruit and vegetables in season; selecting cheaper cuts of meat and including pulses as an alternative protein source, and purchasing foods in bulk.

This study is unique in assessing food affordability by comparing actual dietary intake data of individuals with current poor quality diets with the estimated food costs of

an alternative healthy diet. Moreover, dietary information was obtained from self-reported intake using 7-day food diaries, the gold standard measure (Hoidrup et al., 2002) and dietary data were examined for accuracy of reporting. These food diaries include detailed information about food choices not available from a FFQ. Total cost per energy unit was calculated offering an alternative basis of comparison, and likely under and over-reporting of food consumption was also assessed. All four individuals identified as under-reporters spent less than the mean cost of the modified Mediterranean diet. They represented 50% of those for whom the Mediterranean diet appeared to be more expensive. These reporting inaccuracies are common and imply that food expenditure for these participants were almost certainly greater than reported. Studies have indicated that reported energy intake ranges from 20 to 37% less than measured energy expenditure (Trabulsi et al., 2001). When comparing the total daily cost per MJ, thereby eliminating the differences in energy intake of SMILES participants and the energy contribution of the modified Mediterranean diet, the Mediterranean diet was cheaper for 80% of the participants.

Whilst depression is a condition associated with appetite changes, the poor quality diets of study participants are likely reflective of dietary habits of the general population most of whom fail to meet National Dietary Guidelines (Australian Bureau of Statistics (ABS), 2009). Possible generalizability of the study results to other individuals with MDD, and poor quality diet is uncertain in view of the small sample size. However, given the 7-day food diary technique employed, 133 person days of diet information was captured. As the 7-day food diaries lacked detailed product information, food expenditure was calculated based on medium cost products (incorporating a sensitivity analysis) using prices from the two supermarket chains that make up the dominant share of the national grocery market and incorporated 'reasonable' assumptions on purchase volumes. These limitations could be addressed in future studies by obtaining shopping receipts, or requesting individuals record location of purchase (example, farmers' market, supermarket) as well as reporting product brand and purchase volume. In applying the same approach to the costing of the poor quality diet and the recommended Mediterranean diet, the possible error in the comparison was minimised.

Conclusion

Food costs are a commonly reported barrier to healthy eating, yet this study demonstrates that a healthy diet does not have to cost more than a poor quality diet, which is common in people with MDD as well as the wider community. If food cost is not a major hurdle to healthy eating this clearly focuses attention on other barriers to healthy eating. For example, individuals with

depression typically have reduced motivation to engage in healthy dietary habits (Anton and Miller, 2005), a reduced desire to cook and prepare meals (Darnton-Hill, 1992); and depleted energy for activities such as grocery shopping, meal preparation, and clean-up (Anekwe and Rahkovsky, 2013; Ryden et al., 2008). Individuals may also find the challenge of learning new recipes or developing cooking skills overwhelming (Anekwe and Rahkovsky, 2013; Ryden et al., 2008).

Given that fatigue is a prominent symptom of MDD, the extra effort involved is a disincentive to healthy food preparation. Cooking skill is positively associated with consumption of fruit and vegetables and negatively associated with consumption of convenience foods (Anekwe and Rahkovsky, 2013). As such, providing education and nutritional counselling on preparing nutritious convenient meal ideas on a budget could form part of an integrated care package for people with clinical depression, which may in turn translate into improved dietary patterns and better health outcomes (O'Neil et al., 2013; Opie et al., 2014). Further, it's a common perception that healthy foods are more expensive than less healthy foods and this perception, real or hypothetical, may prevent individuals from choosing healthy foods. Many clinicians have accepted this view point, potentially based on the conflicting evidence available, which may influence their recommendations to patients' regarding food choices. Hence, it is imperative that clinicians are provided with the correct information on this matter when supporting their patients to adopt a healthier diet.

These study findings suggest that the adoption of a healthy modified Mediterranean diet does not cost more (and may cost less) than a poor quality diet. Thus, food cost is not a barrier to healthy eating. This is an important public health message that should be promoted at an individual and population level to encourage improvements in dietary habits. It is desirable that public health messages and nutrition consults incorporate practical strategies for selecting healthy nutritious foods on a budget as well as simple and convenient ways for including these foods in the diet. Addressing these barriers to healthy eating will help improve wellbeing, and achieve desired dietary goals for preventing and managing chronic disease.

Conflict of Interest

The authors have not declared any conflict of interest.

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Full Length Research Paper

Internet-based interventions for pain management: A systematic review of randomised controlled trial (RCTs) conducted from 2010 to 2014

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Limited access to pain management programs was identified as one of the hindering factors in pain treatment. Several internet-based interventions have been developed to improve accessibility. A systematic review of trials of such programs in 2010 documented a preliminary promising effect. A PubMed electronic search was used to identify a systematic randomized controlled trail (RCTs) published 1 January, 2010 to 4 November, 2014 that examined the effectiveness of internet-based pain management programs. The methodological vigorousness of trials was assessed by Jadad scoring system. Out of the 20 RCTs, 5 were on chronic pain, 2 were on acute non-specific pain, while 13 were on disease related pain (rheumatological and neurological diseases, burns, post-operative and cancer-related). Most studies had moderate methodological quality and showed consistent results with respect to effectiveness of internet based programs in reduction of pain, improvement in functionality and psychological well-being. Whilst the current systematic review found a significant pain reduction attributed to internet-based pain interventions further, high-quality RCT are needed to confirm such promising findings.

Key words: Pain, ache, migraine, sciatica, headache, management, treatment, technology, computer, computer-based, internet, internet-based, web, web-based, virtual.

INTRODUCTION

The International Association for Study of Pain (IASP) defines pain as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage” (IASP, 1994). It is important to note that pain is an individual’s experience with an emotional variable attached to it. Thus, management of pain must take this fact into account.(Meredith et al., 2006) Depending on the type of

pain; chronic pain, defined as pain which persists a month beyond the usual course of an acute disease or a reasonable time for an injury to heal, or is associated with a chronic pathological process which causes continuous pain, or pain which recurs at intervals for months or years(Liddle et al., 2004), which seriously affects the quality of social life and working lives of people living in developing world (Breivik et al., 2006). The management

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of unrelieved pain continues to be a major public health issue. Even with the advancement in neurophysiology and pharmacology, this does not help to relieve the pain (European Federation of the International Association, 2004; Boulanger et al., 2007; Statistics Canada, 2008). Literature shows that the economic burden of unrelieved pain is higher than heart disease, cancer and diabetes (Phillips and Schopflocher, 2008). Studies shows that there are many reasons that hinder the cost effective management of unrelieved pain which are lack of knowledge of health professionals, under reporting and limited access to pain management program (Upshur et al., 2006; Peng et al., 2007; Lohman et al., 2010).

Recent studies focused on the management of pain through self employed means, which encourages participating patients to efficiently manage their pain, gain knowledge about the disease and give them confidence to effectively indulge themselves in self employed means (Wagner et al., 1996; Adams et al., 2006). Self employed means the use of internet based intervention, that is both cost-effective and user friendly (Bodenheimer et al., 2002). Literature showed that self management through internet based intervention has become a popular choice in the management of chronic diseases. There are different program designs that have been used by different researchers (Coleman et al., 2010). Internet based programs range from information through website, health risk assessment tools, internet-delivered psychosocial therapies, and multidimensional self-management support programs for children, adults and elderly (Eng et al., 1999).

Previous review conducted in 2010 reported that internet-based interventions seem promising for people in pain (Bender et al., 2011). As with the growing population, the need for cost-effective methods that can reduce the traveling cost, increase the knowledge and confidence of managing the unrelieved pain and also positive change of individual in terms of both behavioral and clinical outcomes are in high demands (Fox, 2008). Literature shows that internet based program can meet the population unmet demands (Gerber, 2006; Fox, 2008).

This review aims to analyze the impact of new management practices and ever evolving means like mobile and internet from 1 January, 2010 to 4 November, 2014 in order to understand the role of this recent development in managing pain of children, adults and elderly. This review will synthesize the newly emerging evidence that involve broad range of internet based intervention in broader age group with broader range of diseases including migraine, sciatica, osteoarthritis, rheumatic arthritis, burn pain and others as all these types of pain badly impact the social and economic aspects of one's' life. Additionally, this review will expand upon previous review (Bender et al., 2011) by profoundly probing the recent literature for diverse internet-based interventions. We have tried to expand the findings of these two earlier syntheses by including the evidences

from more studies, and by including multidimensional effects of internet based intervention on these diverse groups of pain.

METHODOLOGY

An electronic search for this systemic review was conducted to identify articles in PubMed that met our inclusion criteria. The following key words were searched with Boolean words OR and And: Pain, ache, migraine, sciatica, headache, management, treatment, technology, computer, computer-based, internet, internet-based, web, web-based and virtual. Each type of pain was added with Boolean phrase with different terminologies like management, treatment, computer based, internet based and others. The same process was included for all the types of pain mentioned above. Inclusion criteria were publications in English language; publication in a peer reviewed journal; clinical trials published from 1 January, 2010 to 4 November, 2014. Initially, 899 articles were retrieved but after reviewing the titles only 51 articles met the inclusion criteria. Full text articles were retrieved for only those studies that were considered relevant by reviewer after reading abstracts. In depth, probing of full text articles were conducted by the reviewer to check that the articles have described different kinds of internet based intervention, including broad range of disease such as migraine, multiple sclerosis and other, has wide range of age group that involved children, adults and elderly, random allocation of study participant in intervention and control arm. Reviewer then selected relevant articles from the 51 articles and extracted information on many important variables in order to get in-depth knowledge of articles, and to reduce the chances of omitting relevant articles. After an in-depth review, 20 articles were selected. Jadad Scale was used to assess the methodological quality of trials, and high quality on the basis of Jadad Scale was assessed (Figure 1).

RESULTS

Our systemic review highlighted that out of 20 studies included in this review, 9 studies were on chronic pain, 2 were of sub acute pain, 4 were related to rheumatoid arthritis, osteoarthritis and joints pain. Other studies were related to multiple sclerosis, burn pain, cancer and cardiac surgery related pain (Kroenke et al., 2010; Miller et al., 2010; Miller et al., 2011, Martorella et al., 2012)

Description of studies

The sample size of the included studies varies from 26 to 2,480. All the studies included in the review were published between 2010 and 2014. Wide geographical variability can be seen among the selected studies. The studies are from UK, USA, Canada, Germany, Indiana and Jordan etc. The duration of internet based intervention varied from minimum of 7 days and a maximum of 9 months (Table 1).

Description of participants

Most studies targeted patients with chronic pain

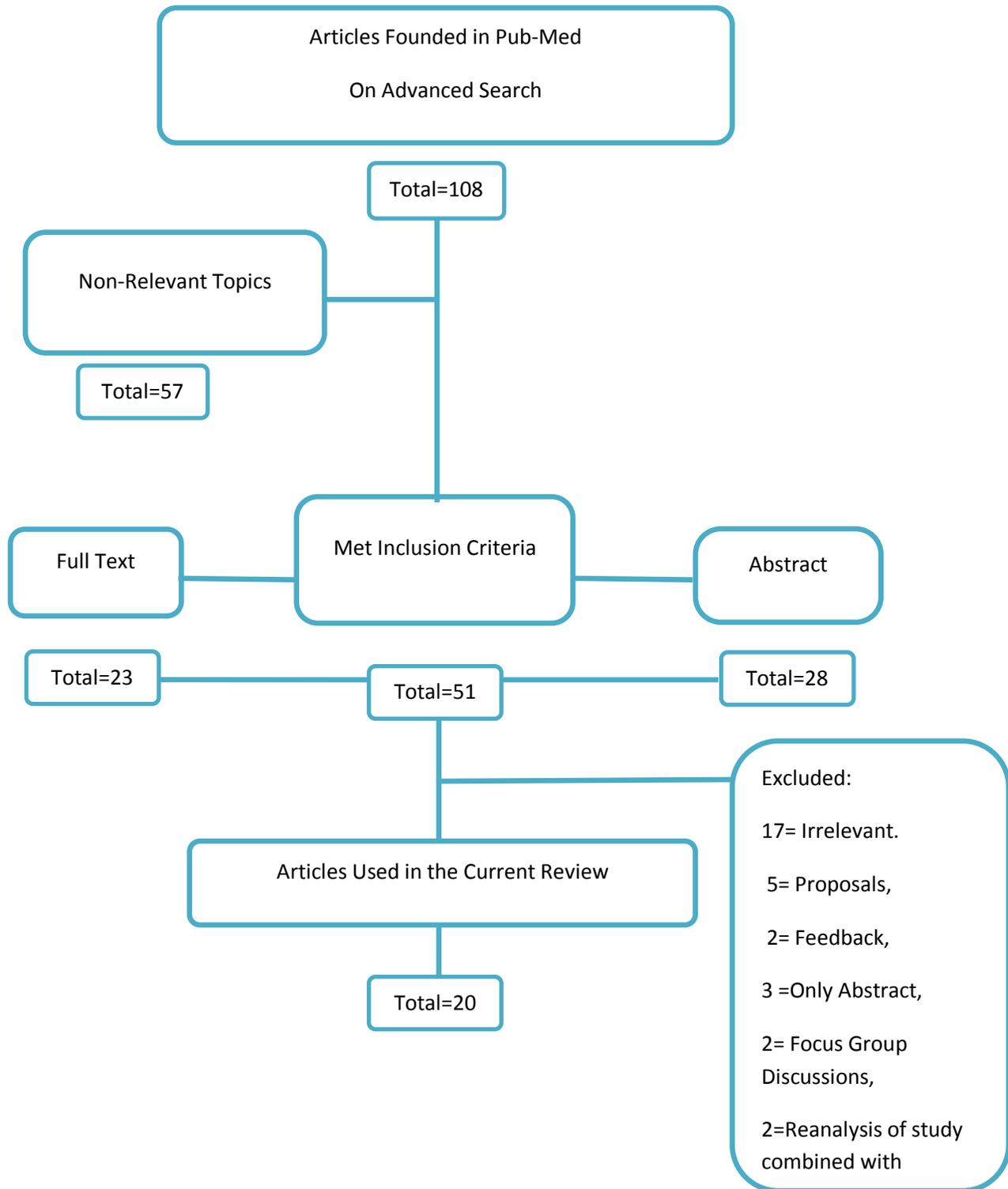


Figure 1. Flow chart of the systematic review.

syndrome including low back pain, migraine, fibromyalgia and musculoskeletal pain (Table 1). Wide age range used in these studies captures adults, elderly and children between 3 years and above. However, one study

only focused on children that were having acute burn pain (Miller et al., 2011). Socio-demographic characteristics of participants were reported by all the studies (Table 1).

Table 1. Selected characteristics of studies evaluating internet-based interventions for pain.

Study	Recruitment (Institution/Countries)	Condition	N	Age in years	Intervention	Control	Program length	Withdrawal
kerin (2012)	Department of veterans Affairs	nonspecific chronic back pain	229	51.2 (mean)	Pedometer access to a website that provided automated walking goals, feedback, motivational messages, and social support through an e-community	usual care	6, 12 months	10%
Ruehlman (2012)	USA	Chronic pain	305	19-78	Online chronic pain management program	wait-listed	7 and 14 weeks	21% 7 weeks 26.1% 14 weeks
Chiauzzi (2010)	Urban Medical School, USA	Chronic back pain	209	46.14	Interactive self-management Website	Standard text-based material	6 month	27% intervention, 16% controls
SE Lamb (2010)	Fifty-six General Practices, UK	Subacute and chronic LBP	701	54 (mean)	AM plus group-based, professionally led CBA	AM in general practice	12 months	15 %
Mahmoud (2013)	Department of Rehab Medc, King Abdullah University Hospital, Jordan	Chronic LBP	100	18-65	Multidisciplinary rehabilitation	Therapist-assisted exercise	36 hours and 40 minutes (6weeks)	
Emily (2012)	Academic Medical Center, USA	Chronic pain	26 adolescent-parents	11-17	Online behavioral pain management intervention	Standard medical care		7.7%
Carpenter et al. (2012)	Internet bulletin boards and advertisement, Seattle	LBP	164	>21	Web-based CBT self-help intervention	Wa\$it-list control	6 weeks	14% baseline 7.03% at 3 rd week 11.5% at6 week
Davis (2013)	USA	FM	79	>18	12-module online intervention MSER	FM patient assign to HT	6-week	37% MSER 51% HT
Bromberg (2012)	website postings electronic newsletter in Neuro centers, USA	Migraine	189	18-65	Web intervention	No treatment	6 months	Less than 100% for intervention 80% control
Buhrman (2013)	Registry, Sweden	residual pain problem	72	40.1(mean)	Guided Internet-delivered CBT	Participate in a moderated online discussion forum	8 weeks	22%

Table 1. Contd.

del Pozo-Cruz et al., (2013)	University Preventive Medicine Service, Spain	acute non-specific LBP	100	18-64	Video demonstration on proper sitting posture and related educational exercises	usual care	9 months	8% intervention 12% control
Simon (2012)	Insurees of a German sickness fund, Germany	depression or acute LBP	2480	20-40	PD	SPI	3 months	73%
Miller (2011)	SPPBC, Australia	acute burn care	40	3–10 years	MMD Group (combined protocol of procedural preparation and distraction)	SD Group		0%
Géraldine et al. (2012)	Cardiac surgery unit of the CHUM, Canada	first cardiac surgery	60	64 (mean)	SOULAGE-TAVIE	usual care, including an educational pamphlet and postoperative follow-up	7 day	13.3%
Miller et al. (2011)	Cleveland Clinic's Mellen Center, Ohio	MS	206	48.1(mean)	Secure electronic messaging plus the new MCCO components	Usual care	12 months	18.9%
Kurt et al. (2010)	INCPAD trial, Indiana	Depression and cancer-related pain	405	58.7(mean)	Centralized telecare management by nurse-physician specialist team with automated home-based symptom monitoring by interactive voice recording	Usual care	12 months	Withdrawal at 1 st month=11.9% 3 months= 16.3 % 12 month= 15.9% in both groups
Elander et al. (2011)	Haemophilia Society, UK	joint pain secondary to hemophilia	196	51.1(mean)	DVD intervention	Control were given booklet only	6 months	44.89%
Stinson et al. (2010)	Tertiary-level centers in Canada, Canada	Idiopathic arthritis	46	12 to 18	Internet intervention self-management program of disease-specific information, self-management strategies, and social support with telecare support	Usual care	12-week	18.1% from intervention and 20.8% from control
Cheryl et al. (2013)	Nationwide Convenience Sample of Adults, Missouri	RA	106	50 (mean years)	Online, cognitive– behavioral, self-management group program (RAHelp), with weekly telecare support	Wait-list control	10 week	11.3%
Bossen et al. (2013)	Articles in newspapers and health-related websites, Dutch	knee and/or hip OA	199	50.-75	Fully automated web-based	Waiting list control group	12 months	15.6% at 3 month 24.6% at 12 months 46% reached adherence threshold

1 CBA: Cognitive Behavioral Approach, 2 AM: Active Management, 3 LBP: Low Back Pain, 4:FM Fibromyalgia, 5:MSER :Mindful Socio-Emotional Regulation, 6 HT: Health Tips Attention, 7PD: Patient dialogue, 8 SPI :Static Patient Information, 9 SPPB: Stuart Pegg Pediatric Burns Outpatient Centre, 10 MMD: Multi Modal Distraction ,11SD: Standard Distraction, 12 MCCO: Mellen Center Care Online, 13 MS: Multiple Sclerosis, 14 INCPAD: Indiana Cancer Pain and Depression, 15 DVD: Digital Video Disk, 16 RA: Rheumatic Arthritis, 17 OA: Osteoarthritis.

Table 2. Jadad scores of internet-based interventions for pain.

Jadad items	Randomization	Sequence of randomization described	Double blind	Double blinding described	Withdrawals and drop out	Inappropriate randomization	Inappropriate blinding	Total
Score	0/1	0/1	0/1	0/1	0/1	0/-1	0/-1	5
kerin et al. (2013)	1	1	0	0	1	0	0	3
Ruehlman et al. (2012)	1	1	0	0	1	0	0	3
Chiauzzi et al. (2010)	1	1	0	0	1	0	0	3
Lamb et al. (2010)	1	1	0	0	1	0	0	3
Mahmoud et al. (2013)	1	1	0	0	1	0	0	3
Law et al. (2012)	1	1	0	0	1	0	0	3
Carpenter et al. (2012)	1	1	0	0	1	0	0	3
Davis and Zautra (2013)	1	1	0	0	1	0	0	3
Bromberg et al. (2012)	1	1	0	0	1	0	0	3
Buhrman et al. (2013)	1	1	0	0	1	0	0	3
del Pozo-Cruz et al. (2013)	1	1	0	0	1	0	0	3
.Simon et al. (2012)	1	1	0	0	1	0	0	3
Miller et al. (2011)	1	1	0	0	1	0	0	3
Martorella et al. (2012)	1	1	0	0	1	0	0	3
Miller et al. (2011)	1	0	0	0	1	0	0	2
Kroenke et al. (2010)	1	1	0	0	1	0	0	3
Elander et al. (2011)	1	1	0	0	1	0	0	3
Stinson et al. (2010)	1	1	0	0	1	0	0	3
Shigaki et al. (2010)	1	0	0	0	1	0	0	2
Bossen et al. (2013)	1	1	0	0	1	0	0	3

Interventions and control conditions

Different internet based interventions were used in this studies that consist of video demonstration, different module of mind socio-emotional regulation, patients dialogue, multi modal distraction, interactive self-management website, centralized telecare management, SOULAGE-TAVIE and others (Table 1) with wait list control, usual care control, and few studies had given some intervention along with the usual care. (Chiauzzi et al., 2010; Lamb et al., 2010; Elander et al., 2011; Martorella et al., 2012; Buhrman et al., 2013; Davis and Zautra, 2013; Nazzal et al., 2013).

Withdrawal from study

The number of participants that withdrew from the studies ranged from 0 to 73%. Most of the studies were compared with the characteristics of withdrawal. The baseline characteristics were compared with those who withdrew from the study and with those who had completed the study (Table 1).

Methodological quality

Because of validity and reliability, Jadad scale was used to evaluate the methodological quality.

The score has the following components randomization, sequence of randomization, blinding, description of blinding, withdrawal, improper randomization and improper blinding. The highest score is 5. Table 1 shows the result of scoring. Most of the studies included in our review had scored 3 (Gerber, 2006; Lamb et al., 2010, Stinson et al., 2010; Elander et al., 2011; Bromberg et al., 2012; Carpenter et al., 2012; Krein et al., 2013; Kroenke et al., 2012; Law et al., 2012; Martorella et al., 2012; Ruehlman et al., 2012) as blinding was not possible in most of the studies. Only two studies scored less on Jadad score (Miller et al., 2011; Shigaki et al., 2013) (Table 2).

Different scales used in the study

Different variety of scales has been used in different studies to report pain severity, stress and depression, and functional distress due to pain. The scales were VA: visual analogue; SOPA: Survey of Pain Attitudes; FABQ: Fear Avoidance Beliefs Questionnaire; PCS: Pain Catastrophizing Scale; RMQ: Roland Morris Disability Questionnaire; SF:

Short Form-12 mental subscale; 7 DASS: Depression Anxiety Stress Scale; BPI: Brief Pain Inventory; SBST: STarT Back Screening Tool; HRQL: Health-related Quality of Life; MO: Medical Outcomes Study and other (Table 3).

Different intervention and its effects

Chronic pain

The type of intervention varies depending on the different types of chronic pains. One study used website that provided automated walking goals, feedback, motivational messages, and social support through an e-community along with pedometer (Table 1). Other studies used 12-module online intervention Mindful Socio-emotional Regulation (MSER) (Davis and Zautra, 2013). One study used interactive self-management website, (Chiauszi et al., 2010) and others used active management plus a group-based professionally led cognitive behavioral approach (CBA) (Lamb et al., 2010). All these studies reported reduction in pain and improvement in both functional activity and psychological well being. A study by Sarah et al. only reported on the reduction in pain in treatment arm when compared to the usual care control arm (Krein et al., 2013). Study by Nazzal et al reported 25 and 45% reduction in pain on different scales in treatment group and 49 and 25% reduction in disability. This study did not comment on the psychological well-being (Nazzal et al., 2013).

Acute non-specific pain

Two studies focused on the sub-acute non specific pain (Simon et al., 2012; del Pozo-Cruz et al., 2013). One study used video demonstration and other patients dialogue (Simon et al., 2012; del Pozo-Cruz et al., 2013). Del Pazo et al used age range of 18 to 64, while Simons included patients with age range of 20 to 40. del Pazo, reported that significant reduction was reported by participants in pain and disability while positive behavioral changes were found in 9 month of follow up (del Pozo-Cruz et al., 2013). On the other hand, Simons et al., reported the decision making was significantly improved in the participants who were in treatment arm (Simon et

al., 2012).

Osteoarthritis (OA), rheumatoid arthritis (RA) and other related diseases

Elander used DVD (Elander et al., 2011), Stinson used internet intervention self-management program of disease-specific information, self-management strategies, and social support with telephone support (Stinson et al., 2010)]. Shigaki used online, cognitive-behavioral, self-management group program (RAHelp), with weekly telephone support (Shigaki et al., 2013). Bossen used fully automated Web-based intervention (Bossen et al., 2013). Elander, Stinson and Danial reported reduction in pain in intervention group (Stinson et al., 2010, Elander et al., 2011, Bossen et al., 2013). While Shigaki and Bossen also reported positive psychological effects (Bossen et al., 2013, Shigaki et al., 2013). Bossen also reported improved physical activity in intervention group (Bossen et al., 2013).

Multiple sclerosis (MS), Burn, Cancer and Cardiac Surgery related pain

Miller et al designed multi modal distraction (MMD) for acute burn patients of age 3 to 10 years (Miller et al., 2011). Kroenke et al designed centralized telecare management by nurse-physician specialist team coupled with automated home-based symptom monitoring by interactive voice recording or internet for depression and cancer related pain (Kroenke et al., 2010). Miller Debora used secure electronic messaging plus the new MCCO components for patients having MS (Miller et al., 2011) and Geraldine used SOULAGE-TAVIE intervention for patients who had gone for first cardiac surgery (Martorella et al., 2012). Kroenke and Miller also reported reduction in pain intensity in treatment arm and reduction in distress score (Kroenke et al., 2010; Miller K et al., 2011). Miller Deborah reported higher general health-related quality of life (Miller et al., 2011). Martorella reported reduction in pain along with better functioning (Martorella et al., 2012).

DISCUSSION

With this review we took a step forward and included all the recent studies from 2010 to 2014. We included 20 studies that focused on the pain management on different age group of children between 3 to 10 years, 18 to 60 years adults, and more than 60 years elderly (Table 1). Out of 20 studies, 6 studies reported the outcome in terms of pain reduction, improvement in functionality and psychological health (Table 3). The results were consistent across all the studies except that of Chiauzzi

Table 3. Outcomes of internet-based interventions for pain.

Study	Pain	Functioning	Psychological	Cost
Kerin et al. (2013)	At 6 months, average RDQ scores were 7.2 for intervention participants compared to 9.2 for usual care, an adjusted difference of 1.6 (95% CI 0.3-2.8, $P=.02$) for the complete case analysis and 1.2 (95% CI -0.09 to 2.5, $P=.07$) for the all case analysis	Chronic Pain The MOS function measure also suggested greater improvements in function for intervention compared to usual care participants at 6 months	NR	NR
Ruehlman et al. (2012)	The growth rate difference was significant and indicated that the treatment group decreased by roughly 1.63 points more than the control group on PCP-S scale	PCP-EA Battery scales measured, perceived disability and pain-induced fear, produced significant group-by-time interaction effects,	Treatment group experienced a greater decrease in psychological problems relative to the control group	-
Chiauszi et al. (2010)	BPI participants inreported a significantly greater mean decrease in self-reported "worst pain" from baseline to posttest ($t = 2.71, P < 0.05$)	No statistically significant effect of condition over time on physical functioning was noted.	A significant effect of treatment over time for the stress subscale of the DASS ($F3, 197= 3.92, P < 0.01$) participants who used the website reported significantly lower stress from baseline to 3-month follow-up ($t = 3.23, P < 0.01$) and 6-month follow-up ($t = 2.65, P < 0.05$). Website participants had a significantly greater increased use of coping self-statements from baseline to posttest ($t = -2.67, P < 0.05$), 3-month follow-up ($t = -3.19, P < 0.01$), and 6-month follow-up ($t = -2.44, P < 0.05$)	-
Lamb et al. (2010)	The difference between CBA and AM was estimated to be on average 3.2 at 3 months, 4.1 at 6 months and 3.8 at 12 months on Pain self-efficacy	Difference between the treatment arms was estimated to be, on average, 1.1 RMQ points at 3 months, rising to 1.4 and 1.3 RMQ points at 6 and 12 months respectively	(SF-12) The difference between CBA and AM was estimated to be on average 1.3 at 3 months, 2.5 at 6 months, and 0.1 at 12 months on SF 12. The difference between CBA and AM was estimated to be on average 2.6 at 3 months, 3.1 at 6 months and 3.0 at 12 months on FABQ	-
Nazzal et al. (2013)	25% reduction in VAS-pain average in treatment arm and 43 % reduction in McGill average pain	49 % decrease in disability score in the McGill scores and 25% reduction in VAS scores. Extension scores increased by 30% and Flexion by 13%. Work ability was increased to 50% in treatment group	NR	NR
Carpenter et al. (2012)	Significant difference between SOPA –Control, SOPA - Harm-Exercise PCS –Rumination PCS –Magnification in intervention group	Significant improvement in SOPA –Disability SOPA –Medication FABQ -Physical Activity n intervention group	Significant improvement in SOPA –Emotion Self-Efficacy PCS –Helplessness Negative Mood Regulation in intervention group	NR

Table 3. Contd.

Davis and Zautra (2013)	MSEER group reported increasing levels of pain coping efficacy (t=4.52, p<.0001)	MSEER group reported improvement in their ability to stay engaged in social activities despite pain (t=3.45, p<.0008), and marginal improvement in their enjoyment of family relationships (t=1.87, p<.07)	MSEER group showed marginally significant increases in positive affect (t=1.81, p<.07), MSEER participants also recorded decreases in feelings of loneliness (t=-2.70, p<.008) and family-related stress (t=-3.75, p<.0003), and greater stress coping efficacy (t=3.48, p<.0007)	Cost-effective
Bromberg et al., (2012)	Greater reduction in their pain catastrophizing from baseline to post-intervention (t = 3.34, P = .0030), baseline to 3-month follow-up (t = 2.98, P = .0099), and baseline to 6-month follow-up (t = 3.80, P = .0006), compared with control participants	No significant effect of treatment over time was noted	Post-hoc tests revealed significantly greater decrease in depression, as compared with the control condition, from baseline to 3-month follow-up (t = 3.66, P = .0009) and baseline to 6-month follow-up (t = 2.50, P = .0399); significantly greater decrease in stress, as compared with the control condition, from baseline to post-intervention (t = 2.57, P = .0324) and from baseline to 3-month follow-up (t = 3.23, P.0045)	-
Sub acute pain, RA, OA				
del Pozo et al. (2013)	Significant positive effects were found on mean LBP severity scores recorded in the online occupational exercise intervention group (SBST 23% change; 2.12 NNT; 0.80 effect size; -1.01 [-1.790 to 0.118] treatment effect; p = 0.019)	Significant reductions in the risk of chronicity of LBP, measured with SBST, were seen in the intervention group compared with the control group: 60.9% patients in the online occupational exercise intervention group were SBST low-risk at 9 months, compared with 27.9% patients in the control group (p < 0.01)	Significant positive effects were found for stage of change in behavior at nine-month follow up (p < .001)	-
Simon et al. (2012)	-	-	The PD group reported a significantly lower overall decisional conflict than the SPI group (38.7 vs. 45.1; p = 0.028) The largest standardized effect (Cohen's d 0.56) resulted from the preparation for decision-making (PD 59.4 vs. SPI 46.8; p < 0.001)	-
Elander et al. (2011)	Intervention, showed a significant, medium-sized, group _ time effect on pre contemplation, with reductions among the DVD group	-	-	-
Stinson et al. (2010)	In post treatment the experimental group had significantly higher knowledge (p < 0.001, effect size 1.32) and lower average weekly pain intensity (p = 0.03, effect size 0.78)	-	No significant group differences in HROQL, self-efficacy, adherence, and stress post treatment	-
Buhrman et al. (2013)	-	-	Group differences with large and moderate effect sizes (ES) were found immediately post intervention for self-efficacy (ASES; ES 0.92, P _ 0.00001) and quality of life (QLS; ES 0.66, P _ 0.003)	-

Table 3. Contd.

Bossen et al. (2013)	At 3 months significant differences between the intervention and control group with respect to pain (P=.002; d=-0.2), tiredness (P=.04, d=-0.16), and improvements in self-efficacy for pain (P=.008, d=0.17) in favor of the intervention group	3months, participants in the intervention group reported a significantly improved physical function status (difference=6.5 points, 95% CI 1.8-11.2)	Positive self-perceived effect (OR 10.7, 95% CI 4.3-26.4)	-
MS, burn, cancer and cardiac surgery related pain				
Martorella et al. (2012)	Significantly less pain interference when breathing/coughing (P= .04)	Experimental group also exhibited fewer pain-related barriers as measured by the Barriers Questionnaire-II (mean 10.6, SD 8.3)	-	-
Miller et al. (2011)	-	MCCO-original group had higher general health-related quality of life as measured by the Euro-Quality of Life 5 Visual Analog Scale (p %0.04)	-	-
Miller et al. (2011)	Significantly reduced pain intensity (p < 0.001)number of pain adverse events were also reduced (p < 0.05) with the use of the MMD protocol	-	Significant decrease in distress scores (p < 0.001)	Cost effective
Kurt et al. (2010)	Of the 274 patients with pain, 137 patients in the intervention group had greater improvements in BPI pain severity over the 12 months 30%decrease in BPI	-	154 patients in the intervention group had greater improvements in HSCL-20 depression severity over the 12 months50%decrease in HSCL	-

1 VA: Visual Analogue, 2 SOPA: Survey of Pain Attitudes, 3 FABQ: Fear Avoidance Beliefs Questionnaire, 4 PCS: Pain Catastrophizing Scale, 5 RMQ: Roland Morris Disability Questionnaire, 6 SF: Short Form-12 mental subscale, 7 DASS: Depression Anxiety Stress Scale, 8 BPI : Brief Pain Inventory, 9 SBST: STaRT Back Screening Tool, 10 HRQL: Health-related Quality of Life, 11 MOS: Medical Outcomes Study.

et al. (2010) who reported improvement in pain reduction and psychological well being, but could not find statistically significant improvement in physical functioning. Bromberg et al likewise, reported the same findings (Bromberg et al., 2012). Stinson reported reduction in pain intensity but no group difference in self efficacy, adherence and stress (Stinson et al., 2010). Results of our review showed that the internet based intervention have improved over time and recent studies have catered on a wider age range group.

When outcomes' regarding psychological well-being of an individual was compared, consistent

results across all the studies except one conducted by Stinson et al 2010. Unlike the previous review that reported inconsistent results concerning the affects of internet based cognitive behavioral therapy (CBT) on psychological wellbeing (Bender et al., 2010). This inconsistency was explained as variability in the internet based CBT, while in our review, more studies focused on chronic pain of back pain and non-specific, only one study was related to migraine (Bromberg et al., 2012) and one about fibromyalgia (FM) (Davis and Zautra, 2013). Only 3 studies used internet based CBT (Lamb et al., 2010; Carpenter et al.,

2012; Buhrman et al., 2013), while others have used variable techniques to deal with pain. In previous studies out of 17, 11 studies used internet based CBT and had positive outcome (Bender et al., 2010). This review also highlighted the affirmative response of internet based intervention on children with acute burn pain. This study also highlighted the cost-effective nature of the intervention along with the better improvement in pain among young children between 3 to 10 years (Miller et al., 2011). From all the studies included in this review, it has been highlighted that internet based interventions are the new form of

treatment that cannot only reduce the pain, but also improve the functionality and psychological well-being of an individual (Table 3). The reason for this internet-based intervention improved outcome is mainly because of its availability. Readily available nature of internet-based interventions does not only make its usage easy but it also keeps the participants engaged.

This in turn not only divert the attention of an individual from pain intensity but also make an individual independent in controlling their situation with ease and pace (Bender et al., 2010). Internet based interventions improve both physical and psychological well being by keeping them engaged in different forums that can also give additional peer support.

Previous review commented on the limitation of participants' recruitment via newspapers and websites (Bender et al., 2010). Nonetheless, studies included in this review highlighted that only 3 studies have recruited participants from the news paper and website advertisements thus rules out the limitation of volunteer biased that was reported in previous review (Bromberg et al., 2012; Carpenter et al., 2012; Bossen et al., 2013). Most of the studies in this review recruited patients from clinic to highlight the strength of these studies, which show that these patients were in more need of treatment than the volunteered participants. Two studies received low Jadad scores, as in this nature of intervention the blinding was not feasible and comparable. Internet based control condition was not feasible but study conducted in Canada, Spain, UK and Australia used blinding approach but only single blinded approach was practiced as double blinded was not feasible (Lamb et al., 2010; Miller et al., 2011; Martorella et al., 2012; del Pozo-Cruz et al., 2013).

When we compare our review with the previous ones we can see much improvement have occurred and the withdrawal rates of the studies included in our studies are very low except for few studies which have reported high withdrawal rates. Studies having telecare support showed low withdrawal rates. Likewise (Rosser et al., 2009) found significantly lower withdrawal rates in studies with some therapist involvement compared to those with no therapist involved. The high withdrawal rates from few studies suggested that because of ease and distance that the intervention provided, this could lead to high attrition rates (Cuijpers et al., 2008). Future studies should take into account those participants who withdrew from the studies so that better strategies could be planned. But most of the studies reported low withdrawal rates suggesting improved strategies of upcoming therapies with limited span of intervention.

Most of the studies have reported the baseline characteristics of participants this involved male, females and also the elderly. Thus, the limitations of previous studies were that the finding could not be generalized as those which were done on adults and female. But with recent advancement, recent studies have involved both the gender with wide variety of age and wide

geographical involvement (Table 1). Thus through this review, we can see the widespread use of the internet based intervention in all the age group and across many geographical boundaries.

The inherent limitation of systematic review is publication bias; aim to reduce the chances of publication biased, studies which had provided negative and positive outcome were reported. Although, with incorporated articles there could be a chance of incomplete retrieval of identified research and reporting bias. Further limitations are no effect sizes were reported and no follow-up measures were reported. Other limitation of this review is that, as reported by previous review, (Bender et al., 2010) studies should focus on the role of internet based intervention for pain in relation to pharmacological therapy. This loop hole still persists in recent studies hence raises the question as whether internet based interventions are adjuvant or alternative of pain management when compared with pharmacotherapy.

Further limitation of the review is that only two studies have commented on the cost-effective nature of the internet-based intervention (Davis and Zautra, 2013; Miller et al., 2011). Future studies should compare the total cost and bring out some cost analysis report so that comparison in terms of cost can be evaluated.

Implication for practice

All the studies included in the review are from different geographical location that caters to a wide range of age group. Thus with known few limitations, it can be concluded that internet based intervention can play a vital role in the reduction of different kinds of pain and the improvement in functionality and positive effects in psychological well-being. However, it can be said conclusively on which extent these interventions are effective but it can also be said that all these interventions included in this article are helpful in wider age group.

Implication for research

Future studies should focus its perception on individual internet-based intervention, its long term feasibility and effectiveness. Cost-effectiveness of the internet-based intervention should be compared with the cost of standardized treatment in order to estimates its cost effectiveness for introducing this regimen in Third World countries. Also, standard reporting and evaluation guidelines should be formulated for internet based intervention in-order to make comparison more pronounced and logical so that future recommendation can be standardized for all the patients worldwide.

Conclusion

Internet based interventions are said to have alleviate

pain as shown in the 20 articles selected by the reviewers, where 5 studies were on chronic pain, 2 were of sub acute pain and 4 were related to RA, OA, and joints pain, including other studies that were about pain related to MS, fibromyalgia, migrain, burn pain, cancer and cardiac surgery. Most of these studies showed consistent results in reduction of pain, improvement in functionality and psychological well-being. Moreover, the studies based on the selected articles have confirmed results of previous review that internet based intervention of pain management have greatly improved the functional and psychological health of participants as specified and particularized in Tables 1, 2 and 3. Nonetheless, well designed studies are still required to make the treatment standardized all over the world.

Conflict of Interest

The authors have not declared any conflict of interest.

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