

# Adiponectin, Leptin and Objectively Measured Physical Activity in Adults: A Narrative Review

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Submitted: 6 Apr 2016

Accepted: 13 Jul 2016

Online: 7 Dec 2016

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To cite this article: Nurnazahiah A, Lua PL, Shahril MR. Adiponectin, leptin and objectively measured physical activity in adults: a narrative review. *Malays J Med Sci.* 2016;**23(6)**:7–24. <http://dx.doi.org/10.21315/mjms2016.23.6.2>

To link to this article: <http://dx.doi.org/10.21315/mjms2016.23.6.2>

## Abstract

The objective of this study was to compile and analyse existing scientific evidences reporting the effects of objectively measured physical activity on the levels of adiponectin and leptin. Articles related to the effects of objectively measured physical activity on the levels of adiponectin and leptin were searched from the Medline and PubMed databases. The search was limited to 'objectively measured' physical activity, and studies that did not objectively measure the physical activity were excluded. Only English articles were included in the search and review. A total of 18 articles encompassing 2,026 respondents met the inclusion criteria. The eligible articles included all forms of evidence (e.g., cross-sectional and intervention). Seventeen and 11 studies showed the effects of objectively measured physical activity on adiponectin and leptin, respectively. Five and four cross-sectional studies showed the effects of objectively measured physical activity on adiponectin and leptin, respectively. Two out of five studies showed a weak to moderate positive association between adiponectin and objectively measured physical activity, while three out of four studies showed a weak to moderate inverse association between leptin and objectively measured physical activity. For intervention studies, six out of 12 studies involving adiponectin and five out of seven studies involving leptin showed a significant effect between the proteins and objectively measured physical activity. However, a definitive conclusion could not be drawn due to several methodological flaws in the existing articles and the acute lack of additional research in this area. In conclusion, the existing evidences are encouraging but yet not compelling. Hence, further well-designed large trials are needed before the effectiveness of objectively measured physical activity in elevating adiponectin levels and in decreasing leptin levels could be strongly confirmed.

**Keywords:** *physical activity, adiponectin, leptin, cross-sectional studies, intervention study, adults*

## Introduction

Globally, many adults may not perform sufficient physical activity to maintain good health (1). Physical activity can be defined as any bodily movement produced by skeletal muscles that require energy expenditure (2) and it has major impact on health. Increased physical activity level and decreased sedentary time may assist with weight management (3) and reduce the risk of getting chronic diseases which include ischemic heart disease, stroke, type 2 diabetes, hypertension, breast cancer and cognitive

disorder as well as osteoporosis (4–6). There are many mechanisms that may act through the effects of physical activity, which could result in changes to circulating adipokines and cytokines, insulin resistance and blood insulin levels, as well as sex hormone production (7).

Physical activity is able to reduce the amount of adipose tissue which lowers the production of sex hormone, insulin, leptin and inflammatory markers that will decrease the exposure to potentially carcinogenic hormones and peptide as well as reduce many types of cancer risk (7). A reduction in body fat will

increase adiponectin and decrease leptin levels. Physical activity was associated with changes in body weight or body fat which will further affect insulin sensitivity (7). Thus, increased physical activity specifically those with moderate to high intensity may increase adiponectin (8–16) and decrease leptin levels (8–11, 13, 17–20).

Adiponectin, also known as AdipoQ or ACRP30, is a serum protein hormone secreted from white adipose tissue into the circulation, found in high concentrations (21). Elevated concentration of adiponectin is associated with improved insulin sensitivity, reduced lipidemia and reduced inflammatory markers (8). Furthermore, it is reported that serum adiponectin levels are inversely related to body mass index (BMI) (22, 23) and also estrogen levels (22).

On the other hand, leptin is a peptide hormone secreted by adipose tissue which plays a central role in regulating human energy homeostasis (24, 25). It has been proven that the level of leptin in blood serum is higher in the obese, in comparison with both adults and children of appropriate body mass. Moreover, physical activity might effectively reduce adipose tissue mass and also lower the level of leptin in blood serum (26).

Studies exploring the effects of physical activity on circulating adiponectin and leptin level have resulted in inconsistent findings. Therefore, the purpose of this paper is to review published evidence for the effects of objectively measured physical activity on adiponectin and leptin in adults. To our knowledge, such a review has not been published previously.

## Methods

### Literature search

A literature search was conducted for scientific articles published between 2005 and 2015 using computerised databases including Medline and PubMed, in April 2015. The search was initiated using various combinations of the following keywords and terms related to adiponectin, leptin and physical activity as follows: ‘Adiponectin’ or ‘AdipoQ’ or ‘ACRP30’ or ‘apM-1’ or ‘leptin’ or ‘Ob protein’ and ‘physical activity’ or ‘exercise’ or ‘sedentary’ or ‘aerobic’ or ‘training’ and ‘objectively measured’ or ‘accelerometer’ or ‘physical activity energy expenditure (PAEE)’ or ‘pedometer’ or ‘heart

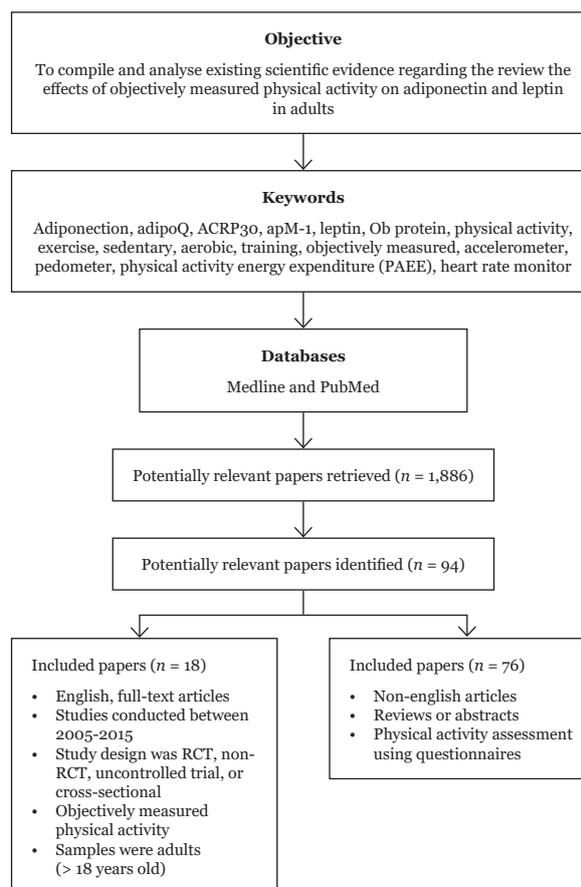
rate monitor’. The reference lists of the retrieved papers and review articles were further hand-searched for additional relevant citations. Unpublished theses were not included in literature search.

### Inclusion criteria

The study design for the included articles could be anything from randomised control trial, non-randomised control trial or cross-sectional study measuring objectively measured physical activity and adiponectin or leptin levels in any tissue human adult subjects (> 18 years old). The articles must be in full-length and published in peer reviewed journals.

### Exclusion criteria

Articles were excluded if they were in non-English language or if they were reviews or abstracts. Articles were also excluded if physical activity assessment was not assessed objectively using calibrated tools.



**Figure 1.** The flow in the literature search process

### Data extraction and analysis

Data on the methodology and outcomes for each study were extracted manually for analysis. The titles and abstracts of the identified articles were screened to eliminate duplicates and unrelated articles. A manual full text review was performed on all articles meeting the inclusion criteria in order to extract information from each article. The extracted information is presented in Tables 1, 2, 3 and 4 which included socio-demographic characteristics and the association or effect of physical activity on adiponectin and leptin.

Article information and respondent demographic distributions were summarised according to the author's name, year of publication, country, age, gender, sample and duration of the study. Additionally, effects of physical activity on adipokines (adiponectin and leptin) were also identified and analysed according to aims/purposes, physical activity assessment method, physical activity category, adiponectin and/or leptin site/assay/CV, analysis adjusted for body or fat mass, final findings and comments. For the outcome comparisons, we focused on cross-sectional and intervention studies on relationship between physical activity/exercise and adipokines (adiponectin and leptin).

## Results

### Articles retrieved

The search generated 1,886 relevant citations 94 were included according to the inclusion and exclusion criteria. Most articles were excluded due to the nature of the studies which focused on subjectively measured physical activity. After the final selection, a total of 18 relevant studies met the inclusion criteria. Socio-demographic characteristics of the respondents are summarised in Table 1 and Table 2. Cross-sectional and intervention studies were included which consisted of six cross-sectional studies and 12 intervention studies. Most articles were based on investigations in the United States of America (19, 20, 27–29). It was obvious that most studies were conducted in developed countries since information was rather lacking from developing and under-developed countries.

### Socio-demographic characteristics

A total of 2,026 respondents were enrolled across 18 studies whereby 961 respondents were involved in cross-sectional studies while 1,065 subjects were recruited for interventions studies.

The respondents consisted of a total 889 men and 1,137 women in which four studies included men only, eight studies included only

**Table 1.** Socio-demographic characteristics of the respondents enrolled in the cross-sectional studies ( $n = 6$ )

First author/ Year	Country	Age/Mean/ Range	Gender	Sample	Duration of study
St-Pierre (2006) (8)	Canada	23.2 ± 3.7 (18.2–35.3)	Female = 63	Non-obese young women ( $n = 63$ )	3 days
Jürimäe (2010) (9)	Estonia	73.5 ± 4.2 (67.0–81.0)	Female = 49	Healthy older females who were taking part gymnastics lessons twice/week for last 5 years ( $n = 49$ )	7 days
Kozakova (2013) (31)	Italy	42.0 ± 9.0	Male = 23 Female = 22	Participants not involve in regular intensive exercise training and competitive sports activity ( $n = 45$ )	7 days
Henson (2013) (32)	UK	63.6 ± 7.7	Male = 364 Female = 194	People at a high risk of type 2 diabetes ( $n = 558$ )	7 days
Green (2014) (27)	USA	24.0 ± 4.8 (19.0–37.0)	Female = 50	Young adult female college student ( $n = 50$ )	7 days
Miyatake (2014) (17)	Japan	Men 44.0 ± 9.7 Women 46.4 ± 8.7	Male = 85 Female = 111	Healthy Japanese not on any medication ( $n = 196$ )	7 days

**Table 2.** Socio-demographic characteristics of the respondents enrolled in the intervention studies ( $n = 12$ )

Author (Year)	Country	Age/Mean/Range	Gender	Sample	Duration
Fatouros (2005) (24)	Greece	69.8 ± 5.1	Male = 50	Inactive men ( $n = 50$ )	12 months
Hara (2005) (12)	Japan	19.2 ± 1.1	Male = 21	Young obese male ( $n = 21$ )	5 months
Marcell (2005) (29)	USA	45.3 ± 8.3	Male = 20 Female = 31	Overweight, insulin-resistant, and nondiabetic individuals ( $n = 51$ )	4 months
Jamurtas (2006) (30)	Greece	31.6	Male = 9	Volunteered overweight males ( $n = 9$ )	48 hours
Kondo (2006) (13)	Japan	18.0 ± 1.5.0 (18.0–23.0)	Female = 96	Healthy Japanese young female students ( $n = 96$ )	7 months
Polak (2006) (18)	France	40.4 ± 6.7	Female = 25	Obese premenopausal women ( $n = 25$ )	3 months
Lim (2008) (14)	Korea	18–71	Female = 74	Healthy young women ( $n = 36$ ) Healthy older women ( $n = 38$ )	10 weeks
Ligibel (2009) (28)	USA	52.0 ± 9.0	Female = 100	Sedentary, overweight breast cancer survivors ( $n = 100$ )	4 months
Saunders (2012) (15)	Canada	25–50	Male = 38	Abdominally obese men ( $n = 38$ )	1 week
Rogers (2013) (19)	USA	56.0 ± 10.5 (30.0–69.0)	Female = 28	Stage I,II or III breast cancer survivors who were post-primary treatment and were not regular exercisers (Intervention = 15, control $n = 13$ )	3 months
Falconer (2014) (16)	UK	59.0 ± 9.7	Male = 184 Female = 101	Adults who had been recruited to the Early Activity in Diabetes ( $n = 285$ )	6 months
Rejeski (2014) (20)	USA	67.0 ± 4.8 (60.0–79.0)	Male = 95 Female = 193	Older, overweight and obese individual at risk for cardiovascular disease ( $n = 288$ )	18 months

women while six studies involved both men and women. The cross-sectional studies enrolled 472 men and 489 women with three studies involved only women and no studies including men only. Interventions studies included 417 men and 648 women with five studies including women only, four studies involved men only while

three studies included both men and women. The respondents studied were of different health status; healthy (8, 9, 13, 17) sedentary and healthy (11, 12, 27, 30, 31) and with health problems (16, 18–20, 23, 28, 29, 32).

### *Relationship between physical activity/exercise and adipokines (adiponectin and leptin) levels*

#### Cross-sectional studies

All studies obtained a fasting blood sample to assess plasma of adiponectin and leptin. An accelerometer was used to measure physical activity in all six studies included. Plasma adiponectin and leptin were mostly analysed by using enzyme-linked immunosorbent assay (ELISA) (10, 31) and radio immune assay (RIA) (8, 9, 17, 27) daily PA in older adults ( $>$  or  $=$  65 years). The intra-assay coefficient of variation (CV) was in the range from 3% to 10% for adiponectin while 10% for leptin. Meanwhile, inter-assay coefficient of variation for adiponectin was from 7% to 15% and leptin was 15%. Out of six studies included, three studies involved analysis adjusted for body or fat mass (8–10). Table 2 summarises the results of these cross-sectional studies. Five studies showed the effects of objectively measured physical activity on adiponectin and four studies on leptin.

Two out of five studies showed a weak to moderate positive association between adiponectin and objectively measured physical activity (8, 9, 32). St-Pierre et al. reported that there was a weak positive association between physical activity and adiponectin ( $r = 0.31$ ) among non-obese young women (8). Among healthy older female Jurimae et al. found similar pattern of association where physical activity was moderately correlated with adiponectin ( $r = 0.438$ ) (9). Meanwhile, among people at high risk of type 2 diabetes Henson et al. showed no association between sedentary times and adiponectin (32). Another study conducted by Kozakova et al. on participants who were not involved in regular intensive exercise training and competitive sports activity reported that physical activity has no association with adiponectin ( $r = -0.08$ ) (31). Green et al. who investigated the associations between objectively measured physical activity, light activity, and markers of cardiometabolic health in young women showed that there were again showed no association between sedentary behaviour, light physical activity and moderate to vigorous physical activity with adiponectin,  $P > 0.05$  (27).

Three out of four studies involving leptin showed a weak to moderate inverse association with objectively measured physical activity (8, 32, 33). Among non-obese young women, St-Pierre et al. reported that leptin was negatively associated with physical activity ( $r = -0.34$ ) (8). Henson et al. who studied on people at high

risk of type 2 diabetes found that leptin showed a significant association between physical activity and leptin ( $P < 0.001$ ) (10). Miyatake et al. again reported there was a significant association between physical activity and leptin among women respondents only ( $P < 0.001$ ) (17). However, Kozakova found no significant association between physical activity and leptin among participants who were not involved in regular intensive exercise training and competitive sports activity (31).

#### Intervention studies

Twelve intervention studies had trial durations of one week to 18 months. A total of seven out of 11 studies included used plasma adiponectin (11–14, 18, 20, 29) while for leptin, three studies used serum (11, 19, 28) and three studies used plasma (13, 18, 20) as their measurement site. All plasma or serum adiponectin and leptin were analysed by using ELISA and RIA, except for Rogers et al. (2013) which analysed total adiponectin and leptin using bead-based immunoassay (MILLIPLEX®). The intra-assay coefficient of variation (CV) used for adiponectin was 0.9% to 9.3% and 3.0% to 8.3% for leptin. Inter-assay coefficient of variation used for adiponectin was 3.0% to 8.1%, and leptin was 3.4% to 8.3%. A total of three studies included analysis adjusted for body or fat mass (18, 19, 28). The results of these studies were summarised in Table 4. Most trials included aerobic exercise that incorporated treadmill walking/running, cycling, swimming, jump rope, and group activities (12–14, 16, 18, 20, 23, 29, 30). The frequency of exercise sessions ranged from two to six times per week. The intensity of aerobic exercise differed across studies with most studies using moderate to high-intensity exercise.

An increase in adiponectin levels following exercise intervention were observed only in six out of 12 studies (11–16). Fatourous et al. found that level of adiponectin increases better on high intensity physical activity compared to moderate intensity physical activity among inactive men ( $P < 0.01$ ) (11). Among young obese men, Hara et al. reported that change in adiponectin level was negatively associated with a decrease in body weight ( $r = -0.664$ ,  $P < 0.001$ ) and body fat mass ( $r = -0.461$ ,  $P < 0.05$ ) due to physical activity intervention (12). Meanwhile, Kondo et al. reported there was a positive association between physical activity and adiponectin ( $r = 0.34$ ) among obese young women (13). Whereas, Lim et al. that included both younger

**Table 3.** Cross-sectional studies of objectively measured physical activity on adiponection and leptin (*n* = 6)

First author / Year / Sample size	Aims/Purposes	Physical Activity Assessment Method	Physical Activity Category	Adiponection Measurement Site / Assay / CV / (ng/ml)	Leptin Measurement Site / Assay / CV / (ng/ml)	Analysis adjusted for body or fat mass?	Findings(s)	Comment (s)
St-Pierre 2006 (8) ( <i>n</i> = 63)	To examine the association between energy balance, use of oral contraceptive pills and other fitness and feeding behaviours with plasma concentrations of ghrelin, adiponection and leptin among young non-obese women.	Participants wore trial-axial accelerometer RT3 to measure physical activity energy expenditure (PAEE).	<ul style="list-style-type: none"> <li>• PAEE 628 ± 192 (191–1021) (Kcal/day)</li> <li>• Physical fitness (VO2peak) 36.8 ± 6.7 (23.3–56.5) (mL/kg.min)</li> </ul>	Plasma RIA Inter-assay CV = < 15% Intra-assay CV = < 10% 8.21 ± 4.79 (2.43–24.6)	Plasma RIA	Yes	<ul style="list-style-type: none"> <li>• There was a positive correlation of adiponection and physical activity (<i>r</i> = 0.31, <i>P</i> = 0.019)</li> <li>• Leptin was negatively correlated with physical fitness (VO2 peak), (<i>r</i> = -0.34, <i>P</i> = 0.006).</li> </ul>	A significant finding of adiponection and PA might suggest that adiponection concentrations may be voluntarily augmented by increasing PA and/or to a greater extent by reducing food intake.
Jurimae 2010 (9) ( <i>n</i> = 49)	To evaluate whether circulating adiponection concentration was associated with physical activity level in healthy older females	Actigraph AM-7164 accelerometer worn for 7 consecutive days	<ul style="list-style-type: none"> <li>• 7,722 ± 3,069 steps/day</li> <li>• MVPA 34.7 ± 23.1 (3.8–83.0)</li> <li>• Light PA 197.0 ± 65.2 (86.0–327.2)</li> <li>• Sedentary PA 547.4 ± 93.9 (383.5–695.3)</li> </ul>	Plasma RIA Inter-assay CV = < 7% Intra-assay CV = < 7% (16.0 ± 6.1)	None	Yes	<ul style="list-style-type: none"> <li>• Plasma adiponection concentration was related (<i>P</i> &lt; 0.001) to:                             <ul style="list-style-type: none"> <li>- steps per day (<i>r</i> = 0.438)</li> <li>- leptin (<i>r</i> = -0.443)</li> </ul> </li> <li>• All other correlations between adiponection and MVPA, light PA, sedentary PA and total activity were not significant (<i>r</i> &lt; 0.349, <i>P</i> &gt; 0.001)</li> </ul>	A significant finding in these elderly healthy respondents since 71.4% of them met physical activity recommendation associated with better adiponection concentration.
Kozakova 2011 (31) ( <i>n</i> = 45)	To evaluate the associations of average daily physical activity and bouts of moderate to vigorous physical activity with cardiovascular and metabolic measures.	Single-axis accelerometer to monitor ambulatory movements Wearing for 7 days	<ul style="list-style-type: none"> <li>• Sedentary (&lt; 100 counts/min)</li> <li>• Light intensity (100–1952 counts/min)</li> </ul>	Plasma ELISA CV not reported 7.6 (3.1–21.3) (mg/l)	Plasma ELISA CV not reported 8.7 (1.3–45.4) (ng/ml)	No	<ul style="list-style-type: none"> <li>• Plasma adiponection levels were inversely related to minutes spent in MVPA (<i>r</i> = -0.37, <i>P</i> = 0.05)</li> <li>• No significant association between PA and adiponection (<i>r</i> = -0.08) or leptin (<i>r</i> = -0.05).</li> </ul>	No significant association was observed between leptin or adiponection due to limited number of days.
Henson 2013 (32) ( <i>n</i> = 558)	To investigate the association of objectively measured sedentary time and breaks in sedentary time with markers of chronic low-grade inflammation	Actigraphs GT3X accelerometer worn for 7 consecutive days	<ul style="list-style-type: none"> <li>• Sedentary (&lt; 25 counts per 15 seconds) 10.2 ± 1.5</li> <li>• Moderate to vigorous physical activity (≥ 488 counts per 15 seconds) 0.5 ± (0.3–0.8)</li> <li>• Breaks (&lt; 25 counts per 15 seconds) to (≥ 25 counts per 15 seconds) 269.0 ± 64.0</li> </ul>	Plasma ELISA CV not reported 11.3 (8.1–16.4)	Plasma ELISA CV not reported Leptin 9.0 (4.9–15.0)	Yes	<ul style="list-style-type: none"> <li>• Sedentary times positively associated with:                             <ul style="list-style-type: none"> <li>- adiponection (<math>\beta</math> = -0.098 ± 0.053) <i>P</i> = 0.068</li> <li>- leptin (<math>\beta</math> = 0.146 ± 0.043) <i>P</i> = &lt; 0.001</li> </ul> </li> </ul>	Only leptin showed significant results but not adiponection. This might be due to potential bias through acute inflammation among participants that were under risk factors for chronic inflammation.

(continued on next page)

Table 3. (continued)

First author / Year / Sample size	Aims/Purposes	Physical Activity Assessment Method	Physical Activity Category	Adiponectin Measurement Site / Assay / CV / (µg/ml)	Leptin Measurement Site / Assay / CV / (ng/ml)	Analysis adjusted for body or fat mass?	Finding(s)	Comment (s)
Green 2014 (27) (n = 50)	To investigate the associations among objectively measured physical activity, light activity, and markers of cardiometabolic health in young women	ActiGraph GT3X+ accelerometer worn for 7 full days	<ul style="list-style-type: none"> <li>Sedentary time (&lt;150 counts/min)</li> <li>504.0 ± 82.4 (303.7–669.2) min/day</li> <li>Light PA (150–2689 counts/min)</li> <li>315.1 ± 80.3 (141.7–548.1) Min/day</li> <li>Vigorous PA 7.3 ± 8.5 (0.0–96.3) Min/day</li> <li>MVPA 58.5 ± 22.7 (19.6 ± 104.1)</li> </ul>	Plasma RIA Intra-assay CV = 2.9% 11.1 ± 4.9 (4.3–25.7)	None	No	<ul style="list-style-type: none"> <li>No correlation between sedentary behaviour and PA with adiponectin (<math>p &gt; 0.05</math>)</li> <li>Sedentary behaviour (<math>r = 0.10</math>)</li> <li>Light PA (<math>r = -0.20</math>)</li> <li>MVPA (<math>r = 0.04</math>)</li> </ul>	No correlation between sedentary behaviour and PA with adiponectin might be due 74% of respondents had at least one CVD risk factor and 72% were either overweight or obese and analysis for this study did not control for body fat.
Miyatake 2014 (17) (n = 196)	To evaluate the link between circulating leptin levels and physical activity and/or physical fitness in apparently healthy Japanese	Tri-axial accelerometer	<ul style="list-style-type: none"> <li>Men 23.4 ± 15.5 (METs h/w)</li> <li>Women 23.4 ± 12.5 (METs h/w)</li> </ul>	None	Plasma RIA CV not reported	No	<ul style="list-style-type: none"> <li>Weak relationship between circulating leptin levels and PA               <ul style="list-style-type: none"> <li>Men <math>P = 0.0509</math>, <math>r = -0.213</math></li> <li>Women <math>P = 0.0079</math>, <math>r = -0.251</math></li> </ul> </li> </ul>	A significant association was found between serum leptin levels and physical activity in women but not in men. However, the gender difference or a clear mechanism between circulating leptin levels and PA could not be explained.

\* PA = Physical activity; MVPA = Moderate to vigorous physical activity; CVD = Cardiovascular disease

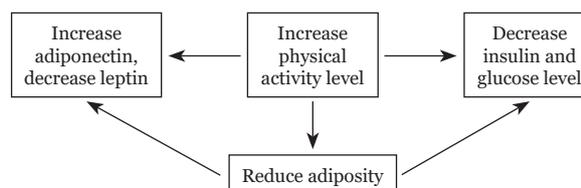
and older women, found adiponectin level increased after a 10-week exercise intervention in older and younger groups (14). Saunders et al. also found that there was a significant increase in adiponectin levels both immediately (high:  $P < 0.005$ ; low:  $P < 0.0001$ ) and 30 minutes after exercise (high:  $P < 0.05$ ; low:  $P < 0.01$ ) among inactive obese men when examining the effect of acute and short-term aerobic exercise training at high intensity and low intensity (23). Falconer et al. reported adiponectin level increased only after six months of physical activity but the effect was limited only among men (16). However, there were six other studies which showed no significant association between physical activity and adiponectin after intervention among various group of subjects (18–20, 28–30).

For leptin, five out of six studies showed a significant effect on objectively measured physical activity. Fatourous et al. found that there was a decrease in leptin level either in low intensity, moderate intensity or high intensity physical activity among elderly males respondents ( $P < 0.01$ ) (11). Kondo et al. also reported a decrease in leptin level after 7-months of moderate intensity of exercise regimen ( $P < 0.05$ ) among healthy young female students (13). Among obese women, Polak et al. reported a significant decrease in leptin level after aerobic training ( $P < 0.001$ ) (18). A study by Rogers et al. showed the association between physical activity and leptin ( $P < 0.05$ ) among breast cancer survivors who were not regular exercisers after three months aerobic intervention (19). However, Rejeski et al. who studied on older, overweight and obese individual at risk for cardiovascular disease reported a significant decrease in leptin occurred when physical activity combined with weight loss compared to physical activity only ( $P < 0.01$ ) (20). Among sedentary, overweight breast cancer survivors, Ligibel et al. reported no association between physical activity and leptin (28).

## Discussion

Physical activity were advantageous to a wide range of adult groups which allowed the control of metabolic dysfunction and restoration to normal levels of adiponectin and leptin which may potentially contribute to a better health outcomes (21). Generally, adiponectin and leptin play an important role in regulation of energy metabolism since both adiponectin and leptin are closely associated with insulin resistance (33).

This review summarises the existing scientific evidence regarding the effects of objectively measured physical activity on adiponectin and leptin. The physiological relationship between physical activity, adipose tissue and adipokines (adiponectin and leptin) level is presented in Figure 2. The increased physical activity might reduce adiposity which would lower the production of insulin, glucose and leptin levels.



**Figure 2.** Relationship between physical activity, adipose tissue and adipokines (adiponectin and leptin)

## Cross-sectional Studies

### Association between physical activity and adiponectin

Review of the included cross-sectional studies shows a positive correlation between objectively measured physical activity and adiponectin (8, 9). This positive correlation might due to high proportions of respondents that met physical activity recommendation which associated with better adiponectin concentration (9). St-Pierre et al. presented a significant positive finding on adiponectin ( $r = 0.31$ ,  $P = 0.019$ ) suggest that adiponectin concentration might be affected by reducing food intake in combination with increasing physical activity (8). Meanwhile, a study by Kozakova et al. evaluated the association of average daily physical activity and bouts of moderate to vigorous physical activity showed no significant association due to a limited number of days (31). Green et al. also presented the same result of no significant correlation between sedentary behaviour and physical activity with adiponectin (27). However it is noteworthy that, 74% of the subjects in the study had at least one cardiovascular disease risk factor, and 72% were overweight or obese. Furthermore, those studies that failed to show a positive association between physical activity and adiponectin levels were not adjusted for body or fat mass.

There are several mechanisms that may act through the effects of physical activity which resulting changes to circulating adipokines,

**Table 4.** Intervention studies of objectively measured physical activity on adiponectin and leptin (n = 12)

First author/ Year/ Sample size	Aims/Purposes	Intervention	Adiponectin and leptin site, assay, CV		Adiponectin		Leptin		Analysis adjusted for body or fat mass?	Findings	Comment (s)
			Pre	Post	P-value	Pre	Post	P-value			
Fatourous 2005 (11) (n = 50)	To investigate leptin and adiponectin responses in elderly males after exercise training and detraining.	<ul style="list-style-type: none"> <li>• 2 sets/exercise (weeks 1–8), 3 sets/exercise (week 8+)</li> <li>Low intensity: 45–50% 1RM, 2 min rest</li> <li>Moderate-intensity: 60–65% 1RM, 4 min rest</li> <li>High intensity: 80–85% 1RM, 6 min rest</li> </ul>	<p><b>Adiponectin</b> Plasma, RIA Intra-assay CV = 6.9% Inter-assay CV = 7.8%</p> <p><b>Leptin</b> Serum, ELISA Intra-assay CV = 5.9% Inter-assay CV = 6.8%</p>	<p>LI: 7.45 ± 2.3</p> <p>MI: 7.79 ± 1.4</p> <p>HI: 7.04 ± 1.6</p>	<p>LI: 8.48 ± 2.16</p> <p>MI: 9.48 ± 1.1</p> <p>HI: 11.36 ± 1.6</p>	<p>ND</p> <p>P &lt; 0.05</p> <p>P &lt; 0.05</p> <p>P &lt; 0.05</p>	<p>LI: 9.1 ± 0.7</p> <p>MI: 8.9 ± 0.6</p> <p>HI: 9.7 ± 0.6</p>	<p>8.8 ± 0.7</p> <p>8.7 ± 0.4</p> <p>7.8 ± 0.6</p>	<p>No</p> <p>P &lt; 0.05</p> <p>P &lt; 0.05</p> <p>P &lt; 0.05</p>	<ul style="list-style-type: none"> <li>• Leptin decreased (3–19%) with training in all exercise groups (P &lt; 0.01)</li> <li>• Adiponectin increased in MI (P = 0.03) HI (P = 0.006)</li> </ul>	<p>The results showed leptin and adiponectin training induced changes are better maintained when a higher (&gt; 80%) intensity was adapted during the preceding training period.</p>
Hara 2005 (12) (n = 21)	To assess major factors regulating adiponectin levels in young obese men	<ul style="list-style-type: none"> <li>• Exercise &gt;30 minutes using treadmills and cycle ergometer 3x/week</li> <li>• 40.8–54.8% VO<sub>2max</sub></li> <li>• 50–60 minutes (after aerobic)</li> <li>• 3 sets/10 reps</li> <li>• 2–3 times/week at 80% 1RM</li> </ul>	<p><b>Adiponectin</b> Plasma, ELISA Intra-assay CV = 3.3% Inter-assay CV = 7.4%</p>	<p>Aerobic 8 weeks: 6.2 ± 2.0</p> <p>Aerobic and resistance training 20 weeks: 3.7 ± 2.2</p>	<p>6.6 ± 2.5</p> <p>4.0 ± 1.9</p>	<p>ND</p> <p>ND</p>	<p>ND</p> <p>ND</p>	<p>ND</p> <p>ND</p>	<p>No</p> <p>ND</p> <p>ND</p>	<ul style="list-style-type: none"> <li>• Change in adiponectin levels was significantly and negatively correlated with decrease in body weight (r = -0.664, P &lt; 0.001) and body fat mass (r = -0.461, P &lt; 0.05) for all subjects.</li> </ul>	<p>The present findings suggest that participation in programs inducing improvement of body composition is more important for young obese men in increasing plasma adiponectin levels than how training is performed.</p>
Marcell 2005 (29) (n = 51)	To determine the effect of exercise training on the levels of C-reactive protein and adiponectin.	<ul style="list-style-type: none"> <li>• Aerobic exercise incorporate 30 minutes of activity 5days/week (at 80%–90% intensities)</li> </ul>	<p><b>Adiponectin</b> Plasma, ELISA Intra-assay CV = &lt; 8% Inter-assay CV = &lt; 8%</p>	<p>Control 15.9 ± 7.0</p> <p>Moderate 14.8 ± 3.9</p> <p>Intense 12.3 ± 4.8</p>	<p>14.0 ± 8.1</p> <p>15.5 ± 4.9</p> <p>13.2 ± 5.8</p>	<p>ND</p> <p>ND</p> <p>ND</p>	<p>ND</p> <p>ND</p> <p>ND</p>	<p>ND</p> <p>ND</p> <p>ND</p>	<p>No</p> <p>ND</p> <p>ND</p>	<ul style="list-style-type: none"> <li>• There were no improvements on plasma adiponectin after exercise training.</li> </ul>	<p>No significant effect of PA on adiponectin levels might be due to moderate-duration of exercise training.</p>

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**Table 4. (continued)**

First author/ Year/ Sample size	Aims/Purposes	Intervention	Adiponectin and leptin site, assay, CV		Adiponectin		Leptin		Analysis adjusted for body or fat mass?	Findings	Comment (s)
			Pre	Post	P-value	Pre	Post	P-value			
Jamurtas 2006 (30) (n = 9)	To investigate the effects of a submaximal aerobic exercise bout on adiponectin and resistin levels as well as insulin sensitivity, until 48 hour post-exercise in healthy overweight males.	<ul style="list-style-type: none"> <li>Perform sub-maximal workout on the cycle ergometer.</li> <li>Exercised for 45 min at an intensity 65% of VO<sub>2</sub>max.</li> </ul>	Adiponectin Serum, ELISA Intra-assay CV = 5.4%	3.6 ± 0.7	3.2 ± 0.45	ND	ND	ND	No	<ul style="list-style-type: none"> <li>Exercise did not result in significant changes in adiponectin.</li> <li>Acute exercise did not affect the levels of adiponectin which might suggest that changes in body composition may be necessary for significant modifications in circulating adiponectin to occur.</li> </ul>	
Kondo 2006 (13) (n = 96)	To determine the effect of exercise on circulating adipokine, high sensitivity C-reactive protein (hs-CRP), and metabolic parameters in obese young women.	<ul style="list-style-type: none"> <li>Cycle ergometer</li> <li>Endurance exercise more than 30 min 4–5 times per week.</li> <li>Fast slope walking/jogging, dumbbells, stretching, cycling, jump rope at 60–70% heart rate reserve</li> </ul>	Adiponectin Plasma, ELISA, CV not reported Leptin Plasma, RIA CV not reported	Obese 16.4 ± 4.6 Control 6.7 ± 1.2	4.2 ± 1.2 8.2 ± 2.3	ND ND	12.3 ± 5.4 6.5 ± 2.2	P < 0.05 ND	No	<ul style="list-style-type: none"> <li>Adiponectin levels were positively correlated with VO<sub>2</sub>max in healthy young women. (r = 0.34, P &lt; 0.05)</li> <li>Circulating leptin and circulating adiponectin increase in (P &lt; 0.01) young obese women after a 7-month moderate intensity exercise regimen.</li> <li>Significant correlation between leptin and adiponectin on PA in obese young women might result through loss of body fat that concomitant with body weight reduction.</li> </ul>	
Polak 2006 (18) (n = 25)	To investigate the effect of aerobic training on gene expression in subcutaneous abdominal adipose tissue and on plasma levels of several adipocytokines in obese women.	<ul style="list-style-type: none"> <li>50% of individual maximal oxygen consumption (VO<sub>2</sub>max)</li> <li>2 sessions per week of supervised aerobic exercise</li> <li>3 sessions per week of home-based exercise on a bicycle ergometer.</li> </ul>	Adiponectin Plasma, ELISA CV = 9.3% Leptin Plasma, ELISA CV = 3.4%–8.3%	10.9 ± 6.1	10.0 ± 4.4	ND	24.3 ± 8.7 18.1 ± 8.3	< 0.001	Yes	<ul style="list-style-type: none"> <li>Plasma leptin declined after the aerobic training program by 25% (P &lt; 0.001)</li> <li>No association between aerobic training-induced changes in plasma adiponectin.</li> <li>No association between aerobic training and plasma adiponectin might show that aerobic training with mild weight loss did not change plasma adiponectin levels.</li> </ul>	

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**Table 4. (continued)**

First author/ Year/ Sample size	Aims/Purposes	Intervention	Adiponectin and leptin site, assay, CV		Adiponectin		Leptin		Analysis adjusted for body or fat mass?	Findings	Comment (s)
			Pre	Post	P-value	Pre	Post	P-value			
Saunders 2012 (15) (n = 38)	To examine the effect of acute and short-term (~1-week) aerobic exercise training on plasma adiponectin levels in inactive, abdominally obese men.	<ul style="list-style-type: none"> <li>Treadmill exercise at 75% of <math>VO_{2peak}</math></li> <li>Low intensity group at 50% of <math>VO_{2peak}</math></li> <li>Performed three bouts of aerobic exercise within one week, with one to two days of rest between each session.</li> </ul>	ND	High: 4.86 Low: 4.47	5.87 5.18	$P < 0.05$ $P < 0.05$	ND ND	ND ND	No	<ul style="list-style-type: none"> <li>HI or LI exercise resulted in a significant increase in adiponectin levels both immediately (High: <math>P = 0.003</math>; Low: <math>P &lt; 0.0001</math>) and 30 minutes after exercise (High: <math>P = 0.0137</math>; Low: <math>P = 0.008</math>).</li> </ul>	These significant findings suggest that an acute bout of aerobic exercise results in a significant increase in plasma adiponectin levels in abdominally obese men.
Rogers 2013 (19) (n = 28)	To determine the magnitude and direction of intervention effect sizes for inflammatory related serum markers and relevant health outcomes	<ul style="list-style-type: none"> <li>Aerobic 150 weekly minutes</li> <li>Moderate intensity monitored by accelerometer and resistance exercise 2 session per week</li> </ul>	Adiponectin Serum, MILLIPILEX, CV not reported, HMWA Serum, ELISA CV not reported	19.8 ± 10.4 (ug/ml) *HMWA 8.8 ± 5.4 (ug/ml)	19.6 ± 10.6 (ug/ml) *HMWA 8.7 ± 5.2 (ug/ml)	ND	46.5 ± 29.1 (ng/ml)	43.9 ± 27.8 (ng/ml)	Yes	<ul style="list-style-type: none"> <li>Effect sizes for HMWA (<math>P = 0.361</math>) and total adiponectin (<math>P = .562</math>) were not significant.</li> <li>Serum leptin was significantly reduced in intervention group (<math>P = 0.031</math>)</li> </ul>	Significant change on leptin in this study might be due to study target which involved longer period of exercise per week.
Falconer 2014 (16) (n = 285)	To investigate whether objectively measured sedentary time was associated with markers of inflammation in adults with newly diagnosed type 2 diabetes.	<ul style="list-style-type: none"> <li>Participants wore uniaxial accelerometer to measure sedentary time</li> <li>Brisk walking for 30 minutes/day</li> </ul>	Adiponectin Serum, ELISA, Intra-assay CV = 5%, Inter-assay CV = 6–7%	Men: 4.4 Women: 5.9 (ug/ml)	Men: 5.4 Women: 5.2 (ug/ml)	$P < 0.05$ $P > 0.05$	ND	ND	No	<ul style="list-style-type: none"> <li>No significant effects of PA on adiponectin found.</li> <li>Adiponectin increased by 23.6% (95% CI 12.4–36.0) after 6 months only in men.</li> </ul>	The increase of adiponectin observed in men might be due to higher MVPA compared to women.

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Table 4. (continued)

First author/ Year/ Sample size	Aims/Purposes	Intervention	Adiponectin and leptin site, assay, CV		Adiponectin		Leptin		Analysis adjusted for body or fat mass?	Findings	Comment (s)
			Pre	Post	Pre	Post	Pre	Post			
Rejeski 2014 (20) (n = 288)	To determine the independent effect of long-term PA and the combined effects of long-term PA with weight loss on inflammation in overweight and obese older adults	<ul style="list-style-type: none"> <li>Walk 30 minutes on most days of the week (with a goal of 150 minutes of aerobic / walking exercise per week)</li> <li>monitored by accelerometer</li> </ul>	<u>Adiponectin</u> Plasma, ELISA Intra-assay CV = 6.5% Inter-assay CV = 3.5% (0.25, 3.9–250 ng/ml)	PA + WL: 7298 ± 621 PA: 614 PA: 6923.0 ± 6731.0 ± 416.0 (ng/ml)	PA + WL: 44.0 ± 3.1 PA: 38.0 ± 2.6 (ng/ml)	PA + WL: 29.6 ± 3.0 PA: 37.3 ± 2.7 (ng/ml)	PA > 0.05 P > 0.05 P > 0.05	PA < 0.01 P > 0.05	No	<ul style="list-style-type: none"> <li>No intervention effect for adiponectin P = 0.13</li> <li>After adjustment for baseline leptin (ng/ml) was significantly lower in the PA + WL (21.3 (95% CI: 19.7–22.9)) compared to PA (29.3 (26.9–31.8)) only. P &lt; 0.01</li> </ul>	Significant effect on leptin in the combined effects of long-term PA and WL on inflammation in overweight and obese older adults might be due to reduction of adipose tissue.

\*ND = Not determine; PA = Physical activity; LI = Low intensity; MI = Moderate intensity; HI = High intensity; HMWA = High molecular weight adiponectin; WL = Weight loss; MVPA = Moderate to vigorous physical activity

insulin resistance and blood insulin levels as well as sex hormone production (7). Many studies have attempted to establish an association between physical activity and adiponectin since physical activity may reduce insulin resistance and glucose metabolism (34). Moreover, plasma levels of adiponectin increased by weight loss and decreased by weight gain (35). Physical activity in combination with diet interventions has been shown to increase adiponectin levels robustly (36). In understanding the association between physical activity and adiponectin, it is essential to consider the duration and intensity of the physical activity procedures used in various studies.

#### *Association between physical activity and leptin*

Leptin showed a weak to a moderate negative association in majority of the studies reviewed. An increased level of physical activity has been found to stimulate energy expenditure, and hence to increase the energy intake required to sustain a constant body mass and body composition (37). Reduced body weight after physical activity is correlated with reductions in plasma leptin concentrations. However, results regarding the effects of exercise on plasma leptin concentrations, independent of fat mass, are conflicting (38).

Leptin was also negatively correlated with physical fitness ( $VO_{2peak}$ ) but not correlated with physical activity (8). Physical fitness and physical activity are usually related, but the concept is different (39). Physical activity has been defined as any bodily movement produced by skeletal muscles that require energy expenditure (2) while physical fitness comprises cardiorespiratory endurance (assessed by either measured or estimated  $VO_{2max}$ ), muscle endurance and muscle strength, both of which are specific to a muscle group and must therefore be measured individually (39). A study by Miyatake et al. found a significant association between serum leptin levels and physical activity in women but not in men (17). However, the gender difference in circulating leptin levels and physical activity could not be explained. Meanwhile, a study by Henson et al. that involved a population at high risk of type 2 diabetes mellitus found sedentary time was significantly associated with leptin could be due to potential bias from acute inflammation among participants that were under risk factors for chronic inflammation (32).

## **Intervention studies**

### *Effect of exercise on adiponectin levels*

It is known that exercise in moderate to high intensity have the largest impact on adiponectin levels. Therefore, several studies have attempted to establish the effects between physical activity and adiponectin levels. Conversely, in inferring the findings of this effect, it is necessary to consider the intensity and duration of the exercise protocols used as well as the variety of the participants involved. A study by Fatourous et al. among inactive men showed that the large increase in plasma adiponectin resulting from the high and moderate intensity resistance training protocol adapted in the study suggests a dose-response effect (11). However, a study by Ligibel et al. presented no significant changes in adiponectin and high molecular weight adiponectin in either group possibly due to a short duration and moderate intensity of exercise intervention (28). Marcell et al. also found no significant effect of physical activity on adiponectin levels which might be due to the moderate duration of exercise training implemented in the study (29).

Most of the studies did not control for weight changes and, therefore, it is still questionable to consider exercise is a modifier of adiponectin. Adiponectin levels decreased with weight gain and increased with weight loss (40). It seems that modifications in body composition or body weight might be responsible for alterations in adiponectin levels. Kondo et al. reported that circulating adiponectin significantly increase in young obese women after seven months adapting to a moderate intensity exercise regimen that might resulted in loss of body fat concomitant with body weight reduction (13). Moreover, change in adiponectin levels was negatively and significantly correlated with a decrease in body weight ( $r = -0.664$ ,  $P < 0.001$ ) and body fat mass ( $r = -0.461$ ,  $P < 0.05$ ) for all young obese men (12). This finding suggest that participation in programs inducing improvement of body composition is more important for obese young men in increasing plasma adiponectin levels than how training is performed. Conversely, a recent study of plasma adiponectin levels in inactive, abdominally obese men showed that both acute and short-term (one week) aerobic exercise training significantly increased plasma

adiponectin without any changes in weight or waist circumference (23). However, it was found that aerobic training with mild weight loss did not change plasma adiponectin levels (18, 20). More studies of resistance training reporting similar outcomes are still needed.

#### *Effect of exercise on leptin levels*

Many studies have evaluated the effect of different exercise protocols on leptin levels due to a multifaceted role of leptin in human metabolism (34). A study by Rogers et al. showed a significant change in leptin could be due to the study design of study which aims longer period of exercise per week (19). Meanwhile, a study by Rejeski showed a significant effect of leptin on the combined effects of long term physical activity and weight loss among overweight and obese older adults (20). This significant change might be due to reduction of adipose tissue. Moreover, a study by Fatouros et al. reported leptin decreased with training in all exercise groups (low intensity, moderate intensity and high intensity) (11). However, the results showed leptin training-induced changes are better maintained when a higher (> 80%) intensity is adapted during the preceded training period.

#### **Strength and Limitations**

This is the first review paper that presents the effects of objectively measured physical activity on adiponectin and leptin among adults which might provide better insight on the association of physical activity and adipokines (adiponectin and leptin). Objective measures such as accelerometer, step counters, and test of cardiopulmonary fitness offer a greater degree of reliability and provide more precise estimates of physical activity compared to self-reported or direct observation. The main drawback of this review was the limited number of included articles since most of the studies were using questionnaires to assess physical activity level. From those included articles, there were several methodological flaws in most of them. Although the studies were conducted worldwide, most were largely concentrated in the Western countries making a global representation impossible in developing or poorer countries. Therefore, more studies using objective measurements need to be conducted

in developing and poorer countries in order to diverse the effect of physical activity on adiponectin and leptin to represent the global population.

#### **Conclusion**

In summary, it is concluded that objectively measured physical activity have potential benefits in improving adipokines (adiponectin and leptin) levels in several health conditions, as proved mainly in cross-sectional studies. Meanwhile, in majority of intervention studies, the association of physical activity and improving of adiponectin levels was not observed. However, the association of physical activity and leptin were observed in majority of the studies. Hence, studies of this nature need to be further investigated and improved before confirmation of the association of physical activity and adipokines (adiponectin and leptin) levels can be strongly substantiated. The necessity well-designed randomised controlled trials which include the use of moderate or high-intensity physical activity of adequate duration to yield the changes in body composition that may increase adiponectin and decrease leptin circulation. The improving of adiponectin and leptin levels may assume to be beneficial for long-term health outcomes. Thus, special attention especially in high risk cohorts that include metabolic syndrome, cardiovascular disease, type 2 diabetes, cancer or overweight should be focussed.

#### **Acknowledgement**

This work was supported by the Ministry of Higher Education Malaysia via Research Acculturation Grant Scheme (RAGS) (RAGS/1/2014/SKK10/UNISZA//2).

#### **Conflict of Interest**

None

#### **Funds**

Research Acculturation Grant Scheme (RAGS) (RAGS/1/2014/SKK10/UNISZA//2).

## Authors' Contribution

Conception and design: MRS, LPL  
Analysis and interpretation of the data: NA, MRS  
Drafting of the article: NA  
Critical revision of the article for important intellectual content: MRS, LPL  
Final approval of the article: NA, MRS, LPL  
Obtaining of funding: MRS  
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