International Journal of Pharmaceutical Sciences and Developmental Research

Butkowski E[1], Brix L[1,2], Al-Aubaidy HA[3], Kiat H[4] and Jelinek HF[1,4]*

[1]*School of Community Health, Charles Sturt University, Albury, Australia*
[2]*Department of Biology, Ludwig-Maximilians-University, Munich, Germany*
[3]*School of Medicine, University of Tasmania, Hobart, Australia*
[4]*School of Medicine, University of New South Wales and Faculty of Medicine and Health Sciences, Macquarie University, Sydney, Australia*

Dates: Received: 16 March, 2016; **Accepted:** 30 March, 2016; **Published:** 01 April, 2016

***Corresponding author:** Herbert F Jelinek, School of Community Health, Charles Sturt University, Albury 2640, Australia, E-mail: hjelinek@csu.edu.au

www.peertechz.com

Research Article

Antidiabetic, Antihypertensive and Statin Medication Use in Metabolic Syndrome

Abstract

Background: Metabolic syndrome (MetS) is characterised by a cluster of metabolic risk factors, which eventually increases the risk of diabetes and cardiovascular disease (CVD). The aim of the current study was to investigate medication use in outpatient communities with respect to the occurrence of these metabolic risk factors as defined by ATPIII.

Methods: Data for this study was obtained from patients attending a diabetes health screening clinic (DiabHealth) in south-eastern Australia between 2005 and 2011. Participants had a medical history taken and anthropomorphic data collected. Participants with three or more MetS factors were classified as MetS positive as outlined by the *National Cholesterol Education Program Adult Treatment Panel III (ATP III)*.

Results: Antidiabetic, antihypertensive and antihyperlipidaemic use varies significantly in uptake by participants and with respect to the number of ATPIII factors present. Blood glucose levels (BGL) and the female waist circumference were significantly better in the MetS compared to the non-MetS group. The most increase in medication use in the MetS group was seen for antidiabetic medication (21.3% versus 2.4%, $p < 0.01$) compared to the non-MetS group. Antihypertensive use tripled (67.8% vs. 26.03%) and Statin use doubled significantly ($p<0.01$) in the MetS group (21.8% vs. 8.9%).

Conclusion: Medication use increases with an increase in ATPIII factors present in the study. Participants with increased BGL (>6.1mmol/L) were not found to have antihyperglycemic medication prescribed. However both antihypertensive medication and Statins were extensively prescribed in cases where only 1 and 2 ATP factors for MetS were present.

Introduction

The metabolic syndrome-definition and prevalence

The metabolic syndrome (MetS) is a cluster of metabolic risk factors associated with a 5-fold increased risk of type 2 diabetes (T2DM) and a 2-fold increased risk of atherosclerotic cardiovascular disease. The *National Cholesterol Education Program Adult Treatment Panel III (ATP III)*'s defined a set of to identify patients having the MetS and viewed CVD as the primary clinical outcome of this disease [1,2]. The 5 criteria identified by the *ATPIII* of which the presence of any three or more comprise the MetS is listed in Table 1 [3].

Table 1: ATP III Modified Clinical Identification of the Metabolic Syndrome.

Risk Factor		Defining Level
Criteria 1: Waist circumference (cm):		
	Men	> 102
	Women	> 88
Criteria 2: Triglycerides (mmol/L)		≥ 1.7
Criteria 3: HDL cholesterol (mmol/L):*		
	Men	< 1.04
	Women	< 1.30
Criteria 4: Systolic Blood Pressure (mmHg)		≥ 130/ ≥ 85
Criteria 5: Fasting Blood Glucose (mmol/L)		≥ 6.1
Use of antidiabetic, antihypertensive or Statin medication		
*HDL – high density lipoprotein.		

Whilst insulin resistance is not a required criterion for MetS using the ATPIII classification, the presence of T2DM or antihyperglycemic medication is considered in its diagnosis [3]. Additional definitions have been recommended by the *World Health Organization (WHO), American Association of Clinical Endocrinologists* and the *International Diabetes Federation (IDF)* [4,5]. Whilst there are some important differences in ranking of the predominant causative factors, there is recognition of similar criteria to the *ATPIII* definition of MetS. However, a major difference between the definition of the *ATPIII* and the *IDF* is the latter does include the patient´s medication as a criterion for the MetS. This additional criterion does allow either BGL or triglycerides to be in the normal range.

One of the most important risk factors leading to T2DM is the presence of prediabetes. Prediabetes is defined by either an impaired fasting (BGL > 6.1mmol/L) or post-prandial blood glucose level (BGL > 11mmol/L). Together with other potential risk factors for CVD, according to the *ATPIII* classification prediabetes is a major cause of the metabolic syndrome and one of its defining factors [6]. Additional underlying metabolic risk factors such as obesity and abnormal body fat distribution account for 20% and 30 % of the adult population and predispose to MetS [7,8]. Although not included in the ATPIII classification, age correlates positively with MetS [9].

MetS and glucose lowering medication

A common finding and independent diagnostic criterion for

MetS is the presence of hyperglycaemia. Whilst the major studies conducted in 2008 and 2009 - UK Prospective Diabetes Study (UKPDS), Veteran's Affairs Diabetes Trial (VADT), Action to Control Cardiovascular Risk in Diabetes (ACCORD), Action in Diabetes and Vascular Disease (ADVANCE) and Rosiglitazone Evaluated for Cardiac Outcomes and Regulation of Glycaemia in Diabetes (RECORD) reviewed the extensive use of antiglycaemic agents as primary strategies in the treatment for MetS, the need for more intensive glycaemic control may also provide cardiovascular benefit for early T2DM with no demonstrated presence of atherosclerosis [10]. If insulin resistance is one of the risk factor in MetS, improving glucose control and insulin resistance through pharmaceutical agents will be another target to be considered in addition to physical activity. However, some drug strategies such as use of metformin for improving insulin resistance are not routinely used for decreasing risk of T2DM and CVD if prediabetes is present [4]. Mixed results have been reported on whether antihyperglycaemic medication decreases CVD risk in patients with prediabetes or T2DM. Only empagliflozin has been shown to improve cardiovascular prognosis. In a recent prospective study, cardiovascular events have not increased with insulin treatment with or without metformin [11,12].

Antihypertensive medication and MetS

Antihypertensive drug treatment is recommended for MetS patients when BP is >140/90mmHg, Observations from the Framingham Risk Study (FRS) state that vascular disorders are central to MetS as indicated that 80% of men and up to 65% of women with hypertension are obese [13]. Insulin resistance has been associated with the development of HT, possibly through a variety of mechanisms involving sodium imbalance, imbalance between the release of nitrous oxide and endothelin-1, insulin action, adipokine activity due to increased adipose tissue and obesity (including perivascular adipose tissue and vascular function), decreased levels of adiponectin, adipokine activity and increased tumour necrosis factor α (TNF-α) [14]. Additionally the importance of genetics cannot be underestimated. Hopkins and Hunt (2003), have provided an extensive review of genetic markers that may contribute to the development of HT [15]. Whilst genetic analysis is still somewhat impractical and economically prohibitive as a diagnostic screening tool, as technology continues to improve these costs will come down.

MetS and statins

The statins are a class of drugs which act to lower total cholesterol and LDL levels by reducing hepatic cholesterol production through inhibition of hydroxyl methyl glutamyl Co-A (HMG-CoA) reductase and a reduced CVD incidence [16]. Statins are also known to reduce circulating triglyceride levels [17]. As a corollary to lowering cholesterol levels the use of statins has also been shown to provide an improvement in eGFR in patients with diabetes, hypertension and glomerular nephritis [18]. As MetS may progress to T2DM and increased CVD it should be considered to be an inflammatory state. The use of statins has been shown to decrease circulating levels of C Reactive protein (CRP), independently to its lipid lowering efect [19].

The successful treatment of MetS involves addressing all of the risk factors treatment regimes. Whilst lifestyle and diet has emerged as a major preventative approach, these changes alone may not control or prevent the development of the risk factors categorising MetS. The current study investigated the use of antihyperglycemic, antihypertensive and lipid lowering (statins) drugs and their associated use in MetS and how medication use differs with respect to the number of MetS factors identified.

Materials and Methods

Data for this study was obtained from patients attending a diabetes health screening clinic (DiabHealth) in south-eastern Australia between 2005 and 2011. Participants were recruited via public media announcements. The screening and data collection were carried out within the School of Community Health at Charles Sturt University (CSU). Participants had a medical history taken and anthropometric data collected in addition to screening for MetS factors. Thresholds for MetS criteria were taken from the definition of the *National Cholesterol Education Program Adult Treatment Panel III (ATP III)* (Table 1). Participants who met three or more criteria were classified as MetS positive. In the current study, medication use was also taken into account in classifying patients into the No MetS or MetS group as described in the definition of the *International Diabetes Federation (IDF).*

Age, gender, body mass index (BMI) (low <20 kg/m^2, normal <25 kg/m^2, overweight 25–30 kg/m^2, and obese >30 kg/m^2 and waist circumference (measured at the midpoint between the lower border of the rib cage and the iliac crest by using a flexible inch tape) were obtained. Blood pressure (BP) measurements were taken using a standard mercury sphygmomanometer and a cuff of appropriate size after the individual had rested for at least five minutes in a supine position. BP was recorded in a sitting position in five individuals with the arm supported at heart height, as this was more comforTable for these five patients. A comprehensive list of prescription medications was provided by each patient. Medication profile for each participant was collected and data sorted into antihypertensive, statin and antidiabetic use.

The data was analysed using R statistical computing (Version 3.2.3 for Windows) and Microsoft Excel (Office2007, Microsoft). All values were expressed as mean ± standard deviation (M±SD). Statistical analysis was performed using an independent sample t-test for two group comparisons of continuous normally distributed data or Chi-square statistics were used to investigate categorical data. In addition proportions analysis was used to compare the data between the five MetS factors. Post-hoc pairwise comparisons were performed using the Benjamini and Yekutieli correction after significant effects were found following the proportions test [20]. ANOVA and post hoc statistics was applied for linical continuous multigroup data. In all tests, $p < 0.05$ was considered to be statistically significant. Power analysis was based on a median effect size and high power, suggesting a sample number of 27 with a p value of 0.05 to be sufficient to establish meaningful differences [21].

Results

During the screening period from January 2005 to October 2011, 1614 volunteers attended the Diabetes Health (DiabHealth) clinic

Table 2: ATPIII factors of the study population.

	MetS	No MetS	p value
WC_Females*	88.8 ±13	94 ± 14.3	< 0.01
WC_Males	101.5 ± 13.2	103.8 ± 11.7	ns
SBP (mmHg)	130.7 ± 17.3	131.5 ± 17.4	ns
DBP (mmHg)	76.1 ± 8.8	76.3 ± 9.1	ns
HDL_Females	1.54 ± 0.4	1.5 ± 0.4	ns
HDL_Males	1.33 ± 0.6	1.2 ± 0.3	ns
Triglycerides (mmol/L)	1.47 ± 0.9	1.42 ± 0.8	ns
BGL (mmol/L)	5.5 ± 1.7	5.8 ± 1.8	< 0.05

*WC: Waist Circumference; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; HDL: High Density Lipoprotein; BGL: Blood Glucose Levels; mean ± standard deviation; ns - non significant.

Table 3: Percentage use of medication for patients with and without metabolic syndrome.

Medication	MetS* (n=239)	(%)	NoMetS (n=292)	(%)	p
Anti-Diabetes	51	21.3	7	2.4	<0.001
Anti-Hypertension	162	67.8	76	26.03	<0.001
Statins	52	21.8	26	8.9	<0.01

*MetS: Metabolic Syndrome present (Factors ≥ 3); NoMetS: Metabolic Syndrome not present (Factors < 3); (%): Percentage.

Table 4: Number of participants using diabetes medication for each MetS factor.

Factor	Dmeds*	Total N	(%)
1	1	106	0.9
2	6	116	5.2
3	21	132	15.9
4	18	80	22.5
5	12	27	44.4

* Dmeds: number of patients on one or more antidiabetic medication.

Table 5: Number of participants using anti-hypertension medication for each MetS factor.

Factor	anti-HT*	Total N	(%)
1	22	106	20.6
2	54	116	46.6
3	81	132	61.4
4	59	80	73.8
5	22	27	81.5

*anti-HT – antihypertensive medication.

Table 6: Number of participants using statins for each MetS factor.

Factor	Statins	Total N	(%)*
1	4	106	3.8
2	22	116	19
3	28	132	21.2
4	19	80	23.8
5	5	27	18.5

*%: Percentage.

at CSU, Albury [22]. Excluding repeat visits, 531 participants had complete data, which was analysed for demographic and clinical attributes, and the five factors of the MetS. All patients with complete data were accepted with no discrimination regarding ethnicity.

Waist circumference for males and SBP/DBP were not significantly different between the two groups (Table 2). Only WC for females was significantly higher in the No MetS group compared to the group with MetS (3 or more of the five factors) (Table 1). Biomarker analysis indicated that HDL, triglycerides and BGL were within recommended limits. BGL was significantly higher ($p < 0.05$) in the No MetS group but still below the cut-off of 6.1mmol/L (Table 1).

Participants were screened for their medication in context with MetS. Groups were divided into no MetS (0–2 factors) and MetS (3-5 factors). Of 531 patients attending the Diab Health screening 70 were clear of any MetS factors and were receiving no antidiabetic, antihypertensive or statin medication.

Antidiabetic, antihypertensive and Statin use combined differed significantly between the MetS and No MetS groups ($p < 0.0001$). When medication use was separated into anti-diabetic, anti-hypertensive and Statins, similar significant differences was found between the MetS and No MetS groups (Table 3).

In the following Tables (Tables 4-6) medication use with respect to presence of MetS factors is shown for antidiabetes (Dmeds) and antihypertension (anti-HT) medication and Statins.

Antidiabetic medication use tripled ($p < 0.001$) when going from No MetS (< 3 factors) to MetS (≥ 3 factors). Comparing medication use with respect to number of ATPIII factors present indicated significant differences ($p < 0.001$) between medication use and the number of ATPIII factors present except between 1 and 2, 2 and 3, 3 and 4, and 4 and 5 factors present (Table 4).

Anti-hypertensive medication also increased significantly with the number of factors considered ($p < 0.001$). However no significant increases were noted when the number of ATPIII factors increased from 3 to 5 (Table 5).

Statin usage increased with the number of MetS factors present. Significant differences in statin use with respect to number of factors present (Table 6) was seen for all comparisons ($p < 0.001$) except when comparing between 2 and 3, 3 and 4 and between 4 and 5 factors present (Table 6).

Comparison of antidiabetic agents, antihypertension medication and Statins in Figure 1 indicates that the antihypertensive class is more prescribed in association with all categories. In general statin use is less prescribed in this population than diabetes in the MetS grop (≥ 3 factors). The use of antidiabetic agents steadily increases and is similar to the antihypertensives once five factors of MetS are present in the patients.

Effectiveness of treatment with respect to MetS factors is shown for the MetS factors indicated by ATPIII (Table 1).

The only significant difference observed was for waist circumference in females when between 1 and 3 MetS factors were

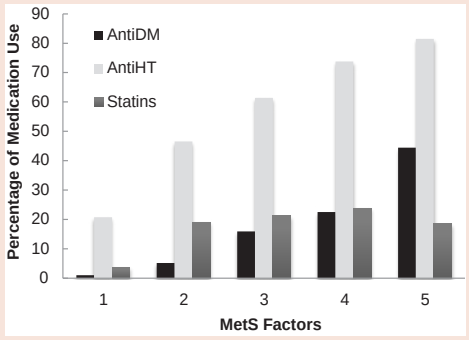

Figure 1: Comparison between Diabetic, anti-HT and Statin use in MetS group.

present ($p<0.01$). However waist circumference for females was at best borderline, observed when 3 ATPIII factors were present and was highest for the group with one MetS factor. Similarly waist circumference for males was only within the desired level if three or four ATPIII factors were present. All other differences in biomarker levels associated with the number of ATPIII factors present showed no significant differences. Triglyceride levels for 5 factors was above the desirable level of <1.7mmol/l [6]. For HDL the desirable levels for females are >1.3 mmol/L and for males >1.04 mmol/L. Only the group with any one of the ATPIII factors present had an elevated mean BGL value (Table 7).

Discussion

ATP III criteria for diagnosis of MetS are practical to use in a clinical setting. According to ATPIII the presence of any three factors (Table 1), constitutes MetS [23]. Management of MetS must first start by addressing factors that are modifiable such as smoking, alcohol use and lack of physical exercise. Prophylactic use of medications such as Statins may also be warranted even on patients with normal cholesterol levels suggested by outcomes from the Heart Protection Study Collaboration (HPS) and the Collaborative Atorvastatin Diabetes Study (CARDS) [24,25]. The most widely recognized of the metabolic risk factors associated with metabolic syndrome are high cholesterol, hypertension, and elevated blood glucose levels. Depending on which factors are present MetS increases the risk of overt diabetes and cardiovascular disease [26]. Drug therapy is essential if modifiable risk factors such as lifestyle practices and diet are not controlling abnormal levels of BGL, systolic blood pressure and cholesterol. The current study investigated the use of medication reported by patients attending a diabetes health screening clinic (DiabHealth) and the presence of single and multiple MetS factors. The study classified MetS as the presence of any three factors of five present as defined by the *ATPIII* classification system but included the use of medication for raised BGL, blood pressure and LDL as an additional criterion as suggested by the *IDF* classification.

The biggest increase of medication when comparing MetS to No MetS (< 3 factors vs ≥ 3 factors) was seen for antidiabetic medication use suggesting that incidence of diabetes may be strongly related to the increase in obesity, blood pressure and cholesterol levels as observed in this study where the mean waist circumference was elevated in the nonMetS group and remained borderline in the MetS group. BGL was significantly different between the two groups but was lower in the MetS group possibly associated with the increase in patients with T2DM and the associated use of antidiabetic medication in the MetS group (Table 3) [23]. Analysis of medication use with respect to the number of MetS factors present indicated that there was no significant increase between any of the biomarkers. Antidiabetic medication use trebled between 2 and 3 MetS factors present and the most significant difference was observed between one and five MetS factors present. This reflects the importance of dealing with hyperglycaemia following the Insulin Resistance Atherosclerosis Study (IRAS), which reported a nearly five times greater risk of coronary artery disease for the group with the lowest insulin sensitivity [1].

Antihypertensive medication was the most often prescribed group (31.1%) compared to the antidiabetic (6.4%) and Statins (19.5%) if only 1 MetS factor of the possible five was present (Table 1). SBP was borderline as recommended by *ATPIII* for factors 0 to 3. A dramatic increase in the mean of SBP to above 140mmHg was seen in association with 4 MetS factors present, which then dropped to ideal levels when 5 factors were present.

Low to moderate-dose statins is the recommended medication therapy for middle-aged patients with a CVD risk of above 10%. For patients with a lower CVD risk statins should be offered selectively and consider patient preference [27]. The current study found that there was a dramatic rise in statin use when the number of MetS risk factors increased from 1 to 2 but then remained steady with a decrease back to the level found with 2 MetS factors present when five factors were present. This result reflects the biomarker levels reported with no significant difference between the No MetS group and MetS group for CVD risk factors apart from waist circumference ($p < 0.001$), which decreased significantly below the MetS cut-off in the MetS group. The cholesterol biomarkers were all within normal limits. Disparities in our study with medication use are associated with our nonspecific categorisation of the MetS characteristics where the presence of one factor can be any one of the five and the presence of three or more the combination of any of the five factors defined by *ATPIII*. Table 7, indicates that only waist circumference is above the cut-off value recommended by *ATPIII*. However SBP and cholesterol levels are below the cut-off due to the use of antihypertensive and statin use. This suggests that preventative measures are having an effect on preclinical MetS (<3 factors present) and BGL, blood pressure and total cholesterol and HDL are controlled in the MetS patient group, which show levels lower than those found in the non-MetS group. Medication use increases with an increase in *ATPIII* factors present in the study. However participants with increased BGL (>6.1mmol/L) were not found to have antihyperglycemic medication prescribed. Both antihypertensive medication and statins were extensively prescribed in cases where only 1 and 2 *ATPIII* factors for MetS were present. Several limitations of the study have to be noted including the self-reporting of medication use and the associated compliance by participants is not verified. In addition confounding factors may play a role in medication use, especially in the non-MetS group who may have only one or two MetS factors present such as economic status and education level.

Table 7: ATPIII biomarker levels with respect to number of MetS factors.

Factors	WCF (cm)	WCM (cm)	Trigs (mmol/L)	HDLF (mmol/L)	HDLM (mmol/L)	SBP (mmHg)	BGL (mmol/L)
1	96 ± 11.5	104.1 ± 13.3	1.41 ± 0.7	1.6 ± 0.4	1.55 ± 0.4	130.9 ± 17.6	6.3 ± 2
2	92.4 ± 16.6	103.4 ± 11.3	1.41 ± 0.9	1.46 ± 0.4	1.47 ± 0.4	131.7 ± 17.4	5.5 ± 1.5
3	88.5 ± 12.7	101.3 ± 13	1.46 ± 1	1.52 ± 0.4	1.51 ± 0.4	131.1 ± 17.7	5.6 ± 1.7
4	89.4 ± 14.4	98.2 ± 12	1.26 ± 0.6	1.6 ± 0.5	1.65 ± 0.4	124.3 ± 14.5	5 ± 1.1
5	91.3 ± 14.9	111.5 ± 19.7	2.1 ± 1.6	1.58 ± 0.2	1.47 ± 0.3	142.3 ± 11.7	6 ± 2.6

WCF: Waist Circumference Females; WCM: Waist Circumference Males; Trigs: Triglycerides; HDLF: High Density Lipoproteins Females; HDLM: High Density Llipoprotein Males; SBP: Systolic Blood Pressure; BGL: Blood Glucose;

Findings in our study indicates that in the focused community of outpatients the metabolic syndrome is relatively well controlled and the majority of the risk factors for CVD are below the documented threshold level. However, waist circumference remains higher than recommended, suggesting that life-style practices may need to be addressed more to achieve an optimum response to the treatment [28]. Statin use may also be below that recommended as the increased SBP and antihypertensive medication use category is quite high (Figure 1) suggesting that there is a high risk of CVD in this population.

Limitation

The South-eastern Australian area has a diverse multicultural population. This study did not discriminate on the basis of ethnicity and therefore further investigations accounting for race may provide additional information.

Acknowledgement

Roche Australia provided the glucose measuring sticks and glucometers. Bev deJong provided technical support.

References

1. Roberts CK, Hevener AL, Barnard RJ (2013) Metabolic syndrome and insulin resistance: underlying causes and modification by exercise training. Comprehensive Physiology 3: 1-58.
2. Huang PL (2009) A comprehensive definition for metabolic syndrome. Disease models & mechanisms 2: 231-237.
3. Grundy SM, Brewer HB Jr., Cleeman JI, Smith SC Jr., Lenfant C (2004) Definition of metabolic syndrome: report of the National Heart, Lung, and Blood Institute/American Heart Association conference on scientific issues related to definition. Arterioscler Thromb Vasc Biol 24: e13-18.
4. Grundy SM, Brewer HB, Cleeman JI, Smith SC, Lenfant C, et al. (2004) Definition of Metabolic Syndrome: Report of the National Heart, Lung, and Blood Institute/American Heart Association Conference on Scientific Issues Related to Definition. Circulation 109: 433-438.
5. Alberti KGMM, Zimmet P, Shaw J (2005) The metabolic syndrome—a new worldwide definition. Lancet 366: 1059-1062.
6. Grundy SM (2012) Pre-diabetes, metabolic syndrome, and cardiovascular risk. J Am College Cardiol 59: 635-643.
7. Grundy SM (2007) Metabolic syndrome: a multiplex cardiovascular risk factor. J Clin Endocrinol Metab 92: 399-404.
8. Grundy SM (2008) Metabolic syndrome pandemic. Arterioscler Thromb Vasc Biol 28: 629-636.
9. Bulhoes K, Araujo L (2007) Metabolic syndrome in hypertensive patients: correlation between anthropometric data and laboratory findings. Diabetes Care 30: 1624-1626.
10. Pelikanova T (2009) [Treatment of diabetes in metabolic syndrome]. Vnitr Lek 55: 637-645.
11. Ferrannini E, DeFronzo RA (2015) Impact of glucose-lowering drugs on cardiovascular disease in type 2 diabetes. Eur Heart J 36: 2288-2296.
12. Hinnen D (2015) Short commentary on empagliflozin and its potential clinical impact. Endocrinol Metab 6: 68-81.
13. Garrison RJ, Kannel WB, Stokes J, 3rd, Castelli WP (1987) Incidence and precursors of hypertension in young adults: the Framingham Offspring Study. Preventive medicine 16: 235-251.
14. Mendizbal Y, Llorens S, Nava E (2013) Hypertension in Metabolic Syndrome: Vascular Pathophysiology. Int J Hypertens 2013: 230868.
15. Hopkins PN, Hunt SC (2003) Genetics of hypertension. Genet Med 5: 413-429.
16. Ebrahim S, Taylor FC, Brindle P (2014) Statins for the primary prevention of cardiovascular disease. BMJ 54: 16; 348.
17. Isley WL, Miles JM, Patterson BW, Harris WS (2006) The effect of high-dose simvastatin on triglyceride-rich lipoprotein metabolism in patients with type 2 diabetes mellitus. Jo Lipid Res 47: 193-200.
18. Sandhu S, Wiebe N, Fried LF, Tonelli M (2006) Statins for improving renal outcomes: A meta-analysis. J Am Soc Nephrology 17: 2006-2016.
19. Averna M, Lo Verde A (2003) Statins and metabolic syndrome. International Congress Series 1253: 243-246.
20. Benjamini Y, Yekutieli D (2001) The control of the false discovery rate in mulitple testing under dependency. Annals of Statistics 29: 1165-1188.
21. Kirby A, Gebski V, Keech AC (2002) Determining the sample size in a clinical trial. 177: 256-257.
22. Jelinek HF, Wilding C, Tinley P (2006) An innovative multi-disciplinary diabetes complications screening programme in a rural community: A description and preliminary results of the screening. Aust J Primary Hlth 12: 14-20.
23. Grundy SM, Cleeman JI, Daniels SR, Donato KA, Eckel RH, et al. (2005) Diagnosis and management of the metabolic syndrome: An American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. Circulation 112: 2735-2752.
24. Colhoun HM, Betteridge DJ, Durrington PN, Hitman GA, Neil HA, et al. (2004) Primary prevention of cardiovascular disease with atorvastatin in type 2 diabetes in the Collaborative Atorvastatin Diabetes Study (CARDS): multicentre randomised placebo-controlled trial. Lancet 364: 685-696.
25. Heart Protection Study Collaborative Group (2003) MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 5963 high-risk individuals: a randomised placebocontrolled trial. Lancet 361: 2005-2016.

26. Rydén L, Standl E, Bartnik M, Van den Berghe G, Betteridge J, et al. (2007) Guidelines on diabetes, pre-diabetes, and cardiovascular diseases: executive summary: The Task Force on Diabetes and Cardiovascular Diseases of the European Society of Cardiology (ESC) and of the European Association for the Study of Diabetes (EASD). Eur Heart J 28: 88-136.

27. (2016) USPSTF2016. United States Preventive Services Task Force. Statin use for the primary prevention of cardiovascular disease in adults: Preventive medication. USPSTF draft recommendation statement.

28. Kaur JA (2014) Comprehensive Review on Metabolic Syndrome. Cardiol Res Pract 2014: 21.

Citation: *Butkowski E, Brix L, Al-Aubaidy HA, Kiat H, Jelinek HF (2016) Antidiabetic, Antihypertensive and Statin Medication Use in Metabolic Syndrome. Int J Pharm Sci Dev Res 1(1): 021-026.*