

World Journal of *Clinical Cases*

World J Clin Cases 2017 September 16; 5(9): 349-372





MINIREVIEWS

- 349 Primary prevention of cardiovascular disease in older adults in China
Yong J, Lin D, Tan XR

CASE REPORT

- 360 Conservative approach to the acute management of a large mesenteric cyst
Leung BC, Sankey R, Fronza M, Maatouk M
- 364 Recurrent aneurysmal bone cyst of talus resulted in tibiotalar calcaneal arthrodesis
Vosoughi AR, Mozaffarian K, Erfani MA
- 368 Anti-N-methyl-D-aspartate receptor encephalitis that aggravates after acinetobacter baumannii pneumonia: A case report
Wang CC, Li DJ, Xia YQ, Liu K

ABOUT COVER

Editorial Board Member of *World Journal of Clinical Cases*, Harrison S Weisinger, PhD, Director, School of Medicine, Faculty of Health, Deakin University, Geelong, VIC 3217, Australia

AIM AND SCOPE

World Journal of Clinical Cases (*World J Clin Cases*, *WJCC*, online ISSN 2307-8960, DOI: 10.12998) is a peer-reviewed open access academic journal that aims to guide clinical practice and improve diagnostic and therapeutic skills of clinicians.

The primary task of *WJCC* is to rapidly publish high-quality Autobiography, Case Report, Clinical Case Conference (Clinicopathological Conference), Clinical Management, Diagnostic Advances, Editorial, Field of Vision, Frontier, Medical Ethics, Original Articles, Clinical Practice, Meta-Analysis, Minireviews, Review, Therapeutics Advances, and Topic Highlight, in the fields of allergy, anesthesiology, cardiac medicine, clinical genetics, clinical neurology, critical care, dentistry, dermatology, emergency medicine, endocrinology, family medicine, gastroenterology and hepatology, geriatrics and gerontology, hematology, immunology, infectious diseases, internal medicine, obstetrics and gynecology, oncology, ophthalmology, orthopedics, otolaryngology, pathology, pediatrics, peripheral vascular disease, psychiatry, radiology, rehabilitation, respiratory medicine, rheumatology, surgery, toxicology, transplantation, and urology and nephrology.

INDEXING/ABSTRACTING

World Journal of Clinical Cases is now indexed in PubMed, PubMed Central.

FLYLEAF

I-V Editorial Board

EDITORS FOR THIS ISSUE

Responsible Assistant Editor: *Xiang Li*
Responsible Electronic Editor: *Li-Min Zhao*
Proofing Editor-in-Chief: *Lian-Sheng Ma*

Responsible Science Editor: *Jin-Xin Kong*
Proofing Editorial Office Director: *Ze-Mao Gong*

NAME OF JOURNAL

World Journal of Clinical Cases

ISSN

ISSN 2307-8960 (online)

LAUNCH DATE

April 16, 2013

FREQUENCY

Monthly

EDITORS-IN-CHIEF

Giuseppe Di Lorenzo, MD, PhD, Professor, Genitourinary Cancer Section and Rare-Cancer Center, University Federico II of Napoli, 80131, Naples, Italy

Jan Jacques Michiels, MD, PhD, Professor, Primary Care, Medical Diagnostic Center Rijnmond Rotterdam, Bloodcoagulation, Internal and Vascular Medicine, Erasmus University Medical Center, Rotterdam, Goodheart Institute and Foundation, 3069 AT, Erasmus City, Rotterdam, The Netherlands

Sandro Vento, MD, Department of Internal Medicine, University of Botswana, Private Bag 00713, Gaborone, Botswana

Shuhei Yoshida, MD, PhD, Division of Gastroenterology, Beth Israel Deaconess Medical Center, Dana 509, Harvard Medical School, Boston, MA 02215, United States

EDITORIAL BOARD MEMBERS

All editorial board members resources online at <http://www.wjnet.com/2307-8960/editorialboard.htm>

EDITORIAL OFFICE

Xiu-Xia Song, Director
World Journal of Clinical Cases
Baishideng Publishing Group Inc
7901 Stoneridge Drive, Suite 501, Pleasanton, CA 94588, USA
Telephone: +1-925-2238242
Fax: +1-925-2238243
E-mail: editorialoffice@wjnet.com
Help Desk: <http://www.f6publishing.com/helpdesk>
<http://www.wjnet.com>

PUBLISHER

Baishideng Publishing Group Inc
7901 Stoneridge Drive,
Suite 501, Pleasanton, CA 94588, USA
Telephone: +1-925-2238242
Fax: +1-925-2238243
E-mail: bpgoffice@wjnet.com

Help Desk: <http://www.f6publishing.com/helpdesk>
<http://www.wjnet.com>

PUBLICATION DATE

September 16, 2017

COPYRIGHT

© 2017 Baishideng Publishing Group Inc. Articles published by this Open Access journal are distributed under the terms of the Creative Commons Attribution Non-commercial License, which permits use, distribution, and reproduction in any medium, provided the original work is properly cited, the use is non commercial and is otherwise in compliance with the license.

SPECIAL STATEMENT

All articles published in journals owned by the Baishideng Publishing Group (BPG) represent the views and opinions of their authors, and not the views, opinions or policies of the BPG, except where otherwise explicitly indicated.

INSTRUCTIONS TO AUTHORS

<http://www.wjnet.com/bpg/gerinfo/204>

ONLINE SUBMISSION

<http://www.f6publishing.com>

Primary prevention of cardiovascular disease in older adults in China

Jian Yong, Dong Lin, Xue-Rui Tan

Jian Yong, Dong Lin, Xue-Rui Tan, First Affiliated Hospital of Shantou University Medical College, Shantou 515041, Guangdong Province, China

Author contributions: Tan XR designed, critically revised and approved the manuscript; Yong J and Lin D conducted the literature reviews, drafted and finalised the manuscript.

Conflict-of-interest statement: The authors state no conflict of interest and have received no payment in the preparation of this manuscript. This paper has been written upon an invitation of the journal editor to the corresponding author.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Correspondence to: Xue-Rui Tan, MD, PhD, Department of Cardiology, First Affiliated Hospital of Shantou University Medical College, No. 22 Xinling Road, Shantou 515041, Guangdong Province, China. tanxuerui@vip.sina.com
Telephone: +86-754-8825218
Fax: +86-754-88259850

Received: January 28, 2017

Peer-review started: February 6, 2017

First decision: May 11, 2017

Revised: May 22, 2017

Accepted: June 12, 2017

Article in press: June 13, 2017

Published online: September 16, 2017

Abstract

Over the past two decades, the percentage of Chinese

who is 60 years or older has increased from 5.2% in 1995 to 10.5% in 2015. Approximately 16% of the population in China was 60 years old and above in 2015. Since 1990, cardiovascular disease (CVD) has been the leading cause of death in China. Cardiovascular medications of older adults are usually more complicated than younger age groups due to polypharmacy, the presence of comorbidities and more susceptible to treatment-related adverse outcomes. Therefore, effective primary prevention of CVD for older adults is important in sustaining the health of older adults and reducing the burden of the healthcare system. Proper management of CVD-related risk factors, such as hypertension, dyslipidemia, diabetes and obesity, can remarkably reduce risks of CVDs in older Chinese. These risk factors can be modified by managing blood pressure, glucose and lipids *via* lifestyle modifications or receiving medications. Smoking cessation, healthy diets, strict alcohol intake and moderate physical exercise are examples of recommended lifestyle changes for remarkably recovering health conditions of older adults who have hypertension, dyslipidemia, obesity, diabetes or complications. Treatment prescriptions of older adults, in general, are recommended to be individualized and to be initiated at a low dose. The future directions for better primary CVD prevention in older adults include establishing guidelines for primary prevention of CVD for different older adults and further research on better management strategies of CVD risks for elderly Chinese.

Key words: Cardiovascular disease; Primary prevention; Adults; China; Aged

© **The Author(s) 2017.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Cardiovascular disease (CVD) is the leading cause of death in China. More than half of the Chinese ≥ 60 years old have been exposed to at least one risk factor for CVD. This review aims to highlight the

primary CVD prevention in Chinese who are 60 years old and above. The management of common risk factors and future directions of primary CVD prevention for elderly population are described in this review.

Yong J, Lin D, Tan XR. Primary prevention of cardiovascular disease in older adults in China. *World J Clin Cases* 2017; 5(9): 349-359 Available from: URL: <http://www.wjgnet.com/2307-8960/full/v5/i9/349.htm> DOI: <http://dx.doi.org/10.12998/wjcc.v5.i9.349>

INTRODUCTION

Cardiovascular diseases (CVDs) have been shown to aggravate the impairment of cognitive, pulmonary, renal, gastrointestinal, and hepatic functions^[1]. Since 1990, CVD has been the leading cause of death in China^[2]. The percentage of the Chinese population who were 65 years old or older has gradually increased from 5.2% in 1995 to 10.5% in 2015, approximately 16% of the people in China were 60 years old and above in 2015^[3]. Although studies over the past two decades have provided relevant information on CVD treatments, the prescription of medications to older adults with CVDs remains challenging to clinicians and governments because older adults usually have polypharmacy, multiple comorbidities, and are vulnerable to adverse effects of treatments^[1,4]. Furthermore, the clinical evidence of CVD treatments for older adults is limited, especially adults who are ≥ 75 years old^[1,5-7]. Numerous studies have suggested that primary CVD prevention for older adults is crucial in sustaining the quality of life of older adults and in reducing the health care burden^[8-10]. Therefore, there has been an increasing interest in primary CVD prevention in older adults.

A considerable amount of literature has been published on the primary prevention of CVD for older adults^[1,9-11]. Since older adults across the world could vary in many aspects, such as physiological conditions, medical history, prior and concomitant medications, lifestyles and environments, the risk factors of each type of CVD and the definition of "elderly" could also differ across older adults worldwide. In China, a person who is 60 years old or above is considered older adults^[5-7]. The primary CVD prevention strategies available in China are for ages, which lacks specific considerations for older adults. Older adults are in general different from younger adults regarding physiological, pharmacokinetics and pharmacodynamics, the susceptibility of adverse drugs effects, and the presence of multiple comorbidities and polypharmacy. Fortunately, there are expert consensus for the management of common risk factors for CVD such as hypertension, dyslipidemia, and diabetes in older or very old people in China. This

review highlights the current primary CVD prevention strategies by briefly describing the management of common risk factors of CVD in China and providing suggestions for future directions, for better primary CVD prevention of Chinese who are 60 years old or above.

MANAGEMENT OF COMMON RISK FACTORS OF CVDs IN CHINA

In China, hypertension, dyslipidemia, diabetes, smoking, and overweight are common high-risk factors of CVDs in older adults^[1,4,12,13]. The 2011-2012 China Health and Retirement Longitudinal Study (CHARLS)^[14] reported that the prevalence of hypertension, dyslipidemia, diabetes, smoking and overweight in Chinese whose age was between 65 to 74 years old were 50%, 64.2%, 19.5%, 25.9% and 30.1% respectively; in Chinese whose age was between 75 years old or above were 65.2%, 59.7%, 28.3%, 17.4% and 22.5%, respectively. Proper managements of these risk factors have been shown to reduce risks of CVDs considerably^[15,16]. A recent study demonstrated that the use of blood pressure and lipids-modulating therapies on hypertension and dyslipidemia patients could potentially prevent 10 to 20 million acute myocardial infarctions^[8]. In 2013, a study on Chinese population reported that managements of blood pressure, lipid and glucose have remarkably reduced risks of CVDs in diabetic patients^[15].

Hypertension

Hypertension has predominantly increased the risk of ischemic heart disease, stroke, kidney failure and aortic diseases in older adults, which are the leading causes of death in older adults^[17]. According to the guidelines of World Health Organization (WHO) in 1999, elderly hypertension is defined as subjects who are aged 60 years or older, systolic blood pressure continuously or 3 measurements of different days at 140 mmHg or higher and/or diastolic blood pressure of 90 mmHg or higher; isolated systolic hypertension (ISH) is defined as systolic blood pressure is at least 140 mmHg and diastolic blood pressure is less than 90 mmHg^[18].

Unlike the younger age groups, the systolic blood pressure of older adults usually increases, and the diastolic blood pressure decreases as they age^[19]. A China survey of 500223 adults over 10 regions in 2013 to 2014 reported that 33.3% of the older adults between 60 years old to 69 years old and 43.7% of the older adults ≥ 70 years old had ISH^[20]. Other types of blood pressure that are also common in older adults in China include high pulse pressure, high fluctuation in blood pressure, masked hypertension, susceptible to secondary hypertension or orthostatic hypotension, and unusual pattern of blood pressure change in day and night^[21,22].

Target blood pressure

An expert consensus for the management of hypertension in the elderly recommended using personalized medicine and setting intermittent goals to treat elderly subjects with hypertension and other diseases such as heart, brain, and kidney functions^[21]. According to the expert consensus, the target of blood pressures for older adults is recommended to begin at < 150/90 mmHg and gradually lowered to < 130/80 mmHg. For patients above 80 years old, their blood pressure is recommended to be under 140/80 mmHg.

The J-curve phenomenon of blood pressure has been increasingly recognized^[23]. Although high blood pressure increases the risk of damaging target organs, excessively lowering blood pressure can influence the blood flow to target organs, which is also harmful to patients^[24,25]. The degeneration of vascular elasticity and autonomic nervous system have been associated with higher risk of organ damage and stroke^[1,12,21]. For older adults who had ISH and ischemic heart diseases, intense blood pressure reduction medications are not recommended to be used in lowering blood pressure^[12,21,22]. Antihypertensive treatments are more effective in patients with higher baseline blood pressure level than those with lower baseline blood pressure^[10,16]. Since anti-hypertensive treatments are usually much effective in reducing systolic blood pressure than in reducing diastolic blood pressure, antihypertensive medications can reduce the blood pressure of older adults with ISH^[12,16,21].

The ideal blood pressure targets for older adults with high cardiovascular risks (such as elderly with coronary artery disease, diabetes, kidney disease and stroke) remain unclear. Most guidelines suggest the blood pressure targets of diabetic older patients should be under 130/80 mmHg, which lacks support from large clinical studies^[5,21]. Chinese expert consensus for the management of hypertension recommended^[21] the optimal blood pressure targets for patients who had kidney disease is recommended to be 130/80 mmHg; for patients who were also ≥ 80 years old, blood pressure is recommended to be under 140/90 mmHg. In patients without contraindications, preferred treatments are ACEI or ARB because these medications can reduce proteinuria, ameliorate kidney functions, and delay the development of kidney dysfunction, decrease the risk of end-stage kidney diseases^[26]. Loop diuretics are recommended for patients with severe kidney functions. Hypertension in the Very Elderly Trial (HYVET)^[16] is the only large study so far that aimed to study patients who have hypertension and are 80 years old or older. That study had 3845 subjects, in which 1526 of them were Chinese patients. That study showed that reducing blood pressure < 150/80 mmHg is beneficial to reduce cardiovascular outcomes. The Chinese expert consensus for the management of hypertension in older adults^[21] suggests that blood pressure can further reduce to < 140/90 mmHg if patients do not

have orthostatic hypotension, fainting, angina, cardiac and cerebral vascular perfusion deficiency, or other abnormal clinical manifestation. Further studies are recommended to assess the benefit of reducing blood pressure down to 140/90 mmHg^[21].

Antihypertensive therapy

The pharmacokinetics of drugs in older adults is usually different from younger adults^[22,27]. Older adults with comorbidities are in general at high risk of treatment-related adverse events such as deterioration in renal function and excessive orthostatic blood pressure decline^[22,27,28]. Therefore, the choice of antihypertensive medication in older adults should consider age-related physiological characteristics that are related to the pharmacokinetics of drugs and the presence of comorbidities^[6,7,22,27,28]. In general, medications should be initiated at the lowest dose and be slowly titrated based on the blood pressure response of patients^[21,22]. The blood pressure of older adults should be gradually reduced to below target level to prevent hypotension that usually causes older adults to have a higher risk of falling and fainting^[21,22,24]. The assessment of blood pressure responses to drugs is recommended to include consideration of adherence to blood pressure medications, potential drug-drug interactions, secondary hypertension, appropriateness of drug choice and accuracy of blood pressure measurement^[10,27]. Many older patients require at least two types of antihypertensive medications to reduce blood pressure^[4,21,27].

The five most common classes of anti-hypertensive treatments are calcium channel blockers (CCB), diuretics, angiotensin receptor blockers (ARB), beta-blockers and angiotensin-converting-enzyme inhibitors (ACEI) are used in treating older adults with hypertension^[16,22]. Diuretics and long-term calcium antagonists are recommended as preliminary treatments for older adults without symptomatic complications because these medications are effective in reducing blood pressure and have little adverse effects^[21].

The recommended essential antihypertensive treatments for older adults currently are dihydropyridine (DHP) calcium channel blockers because they are reliable and effective in reducing blood pressure and can be concurrently used with other 4 classes of drugs^[21]. CCB has the following characteristics^[1,13]: (1) no adverse effect on metabolism, which is appropriate for older adults with diabetes and metabolic syndrome; (2) the effect of reducing blood pressure is not affected by salt intake, which is suitable for salt-sensitive hypertension; and (3) effective on older adults with low renin activity or low sympathetic activity.

The use of diuretics has been associated with the decreased number of cardiovascular events and the reduced risk of cardiovascular mortality^[29]. Thiazide diuretics can be utilized with other anti-hypertensive treatments to reduce the blood pressure in older adults, including older adults with ISH, or heart failure

and edema. Long term usage of diuretics might cause electrolyte disturbance and renal blood perfusion, and increase the risk of glucose and lipid metabolic syndrome; therefore, the change of renal functions and electrolyte levels need to be carefully monitored to prevent the development of hypopotassemia and hyperuricemia^[21]. The use of diuretics in older adults should start at low doses; for those older adults whom their Creatinine clearance rate < 30 mL/min per 1.73 m², loop diuretics such as torasemide and furosemide are recommended^[21].

ACEI is effective in lowering blood pressure and protecting the renal function of older adults who have hypertension and high renin activity^[27]. This drug is suitable for hypertensive older patients who also have coronary artery disease, myocardial infarction, angina pectoris, diabetes, left ventricular dysfunction, chronic kidney disease or proteinuria^[22]. ACEI does not only affect glucose and lipid metabolism, heart rate and cardiac output, but it also leads to little adverse outcomes^[1,13,21]. The main adverse outcomes include coughing, skin rashes; allotriogeusia, kidney function deterioration, angioneurotic edema, and fatality occur in rare cases^[21].

The effect of ARB on lowering blood pressure and protecting kidney function are very similar, lead to fewer adverse outcomes such as coughing, angioneurotic^[27]. This drug is particularly useful in subjects who are susceptible to ACEI-related adverse outcomes^[22]. While using ACEI or ARB medications in older adults, close monitoring their blood potassium and serum creatinine levels are recommended^[21].

Beta-blockers are the pre-ferred choice recommended to hypertensive older adults with coronary artery disease, chronic kidney failure, and without contraindication^[12,21]. Prescribing beta-blockers to older adults with sick sinus syndrome, second degree or higher atrioventricular block or bronchial asthma is prohibited because its long term usage will result in glucose and lipid metabolic disorder^[12,21]. Since bradycardia and atrionector disorder are common in older adults, the usage and dose of beta-blockers should be determined according to their indications^[12,21].

Alpha-blockers are usually not considered as the first choice for hypertensive older adults unless they have benign prostate hyperplasia^[13,16,21,22]. The main adverse outcome is orthostatic hypotension. Therefore, such treatment should be initiated at low doses and eaten before sleep; the orthostatic blood pressure should be monitored to prevent orthostatic hypotension^[21].

Dyslipidemia

Dyslipidemia, including hypercholesterolemia, hypertriglyceridemia, combined hyperlipidemia and low HDL-C, has been associated with increased risks of CVDs^[1,6,13]. The elevation of plasma cholesterol, especially low-density lipoprotein cholesterol (LDL-C) and non-high-density lipoprotein cholesterol (non-HDL-C), are main risk factors for arteriosclerotic vascular disease (ASCVD)^[30,31]. The decrease in

LDL-C has been shown to improve cardiovascular health significantly^[15]. Numerous guidelines, including China, have suggested that modulating LDL-C levels or non-HDL-C can considerably reduce CVD risk^[6,32-34]. Therefore, the guidelines of many countries including China have selected LDL-C as the primary target of lipid-lowering therapy^[32-34]. The guideline of dyslipidemia prevention for Chinese adults^[34] has established target levels of LDL-C and non-HDL-C for different risk groups. Table 1 shows the target lipid levels for older Chinese (men \geq 45 years old or women \geq 55 years old). According to that guideline, if high LDL-C or HDL-C levels cannot be safely reduced to the target level, 50% reduction from baseline is also acceptable.

Lipid-modulating therapy

Over the past decade, a considerable amount of literature has shown that statin is effective in reducing risks of CVDs through modulating blood lipids^[35,36]. For an example, Heart Outcome Prevention Evaluation-3 trial (HOPE-3)^[37] found that the use of rosuvastatin (10 mg, QD) can reduce the risk of cardiovascular events in an intermediate-risk population, regardless of the baseline LDL-C levels. Open Label Study of Long Term Evaluation Against LDL-C Trial (OSLER)^[38] and ODYSSEY^[39] have shown that the use of Proprotein Convertase Subtilisin/Kexin type 9 (PCSK9) inhibitor in addition to statin can further reduce 50% of LDL-C level, leading to 50% reduction in risk of developing CVDs. A systematic review^[40] in 2013 has demonstrated that statin, in comparison to placebo, significantly reduced the risk of myocardial infarction and stroke in elderly subjects without previous CVD by 39.4% and 23.8%, respectively. Furthermore, the HPS2-THRIVE^[41] trial showed that although statin is more effective in lowering LDL-C of Chinese than in Europeans, statin-related adverse effects is also more noticeable in Chinese than in Europeans. Therefore, statin has been suggested as the first line lipid-modulating therapy^[10,35,42]. Statin-related adverse events include cognitive dysfunction, myopathy, increased risk of developing diabetes and cognitive impairment^[32,33]. Whether older adults are more susceptible to adverse effects of statin therapy and whether effects of statin therapy in younger population can be extrapolated to Chinese who are 80 years and above remain unclear^[43]. Hence, statin therapy for older adults has been recommended to be initiated at a low dose and gradually titrated according to the response of patients, especially in Chinese who are 80 years old and above^[2,3,6,27,34,35]. Non-statin therapies can be considered for older adults who cannot tolerate statin or cannot attain target LDL-C level after taken maximum tolerated statin therapy^[44].

Diabetes

Type II diabetes is the most common types of diabetes among older adults in China^[4]. Postprandial hyperglycemia is more noticeable in Chinese patients

Table 1 Target lipid level across different risk groups of older Chinese (men ≥ 45 years old or women ≥ 55 years old)

Current lipid level (mmol/L)	Risk level	Target lipid level (mmol/L)
TC ≥ 7.2 or LDL-C ≥ 4.9	High	Primary target LDL-C < 2.6
$4.1 \leq \text{TC} < 7.2$ or $2.6 \leq \text{LDL-C} < 4.9$ (hypertension + smoking or low HDL-C)		Secondary target
$3.1 \leq \text{TC} < 7.2$ or $2.6 \leq \text{LDL-C} < 4.9$ (hypertension + smoking + low-HDL-C)		
$3.1 \leq \text{TC} < 7.2$ or $1.8 \leq \text{LDL-C} < 4.9$ (diabetes)	Moderate	Non-HDL-C < 3.4
$5.2 \leq \text{TC} < 7.2$ or $3.4 \leq \text{LDL-C} < 4.9$ (smoking or low HDL-C)		Primary target
$4.1 \leq \text{TC} < 7.2$ or $2.6 \leq \text{LDL-C} < 4.9$ (hypertension, or smoking + low HDL-C)		LDL-C < 3.4
$3.1 \leq \text{TC} < 4.1$ or $1.8 \leq \text{LDL-C} < 2.6$ (hypertension + smoking or low HDL-C)	Low	Secondary target
$3.1 \leq \text{TC} < 7.2$ or $1.8 \leq \text{LDL-C} < 4.9$		Non-HDL-C < 4.1
$3.1 \leq \text{TC} < 5.2$ or $1.8 \leq \text{LDL-C} < 3.4$ (smoking or low HDL-C)		Primary target
$3.1 \leq \text{TC} < 5.2$ or $1.8 \leq \text{LDL-C} < 3.4$ (smoking or low HDL-C)		LDL-C < 3.4
$3.1 \leq \text{TC} < 4.1$ or $1.8 \leq \text{LDL-C} < 2.6$ (hypertension or smoking + low HDL-C)		Secondary Target
		Non-HDL-C < 4.1

LDL-C: Low-density lipoprotein cholesterol; TC: Total cholesterol; HDL-C: High-density lipoprotein cholesterol.

with early type 2 diabetes than in other population because they have significant β -cell deterioration^[45]. Chinese is at high risk of developing diabetes with BMI relatively lower than non-Asian patients^[46]. Older adults with diabetes are usually complicated by other metabolism disorders such as high LDL-C, high HDL-C, and hypertriglyceridemia^[7]. Moreover, older adults with diabetes usually have poor treatment adherence and tolerance, and at high risk of hypoglycemia due to the following main reasons^[7,28,47]: (1) damaged autonomic nervous system and sympathetic nervous system; (2) deteriorated compensatory mechanism of blood glucose hormone; and (3) malnutrition, irregular eating habits, reduced cognitive impairment, alcohol consumption, under-reserved hepatic glycogen, polypharmacy, and declined hepatic and renal functions.

Management of diabetes

Higher risks of morbidity and mortality have been found in older adults with diabetes at both low and high glycated hemoglobin (HbA1c) levels^[7]. As a consequence, the Chinese guideline for the management of diabetes^[42] has recommended the control of HbA1c to effectively reducing the risk of morbidity and mortality (Table 2). The target of blood pressure and blood lipid for older adults with diabetes are shown in Table 3. Treatments that have little or no association with hypoglycemia are recommended to reduce blood glucose level of older adults^[48]. Older adults are recommended to have fasting blood glucose level < 7.8 mmol/L and 2-h after fed blood glucose level < 11.1 mmol/L^[48]. Treatment strategies are encouraged to avoid hypoglycemia, symptomatic hyperglycemia, orthostatic hypotension, and other drug-related complications^[7,28,42,49]. Since postprandial hyperglycemia and β -cell deterioration are characteristics of Chinese patients with type 2 diabetes, considerations of anti-diabetic therapy for

Chinese patients with type 2 diabetes include control of postprandial hyperglycemia and β -cell preservation. Older adults usually have lower metabolism rate, malnutrition and multiple comorbidities^[7,28]; therefore, their diets are recommended to limit calorie intake and balance diet nutrition for the prevention of deteriorating other comorbidities^[50]. Older adults with diabetes should avoid high-intensity exercise to prevent hypoglycemia and injury^[28,42]. Intense blood-glucose-lowering therapy such as glyburide should be avoided as treatment options to prevent hypoglycemia^[28,42]. Initial therapy should start at low doses, and insulin therapies must be used with caution. Older adults with diabetes and high risk of CVD are not encouraged to use glycemic agents to lower blood glucose levels^[7,27,50].

In comparison to older adults who had diabetes at a younger age, older adults who developed diabetes at later age secrete more insulin resistance and insulin compensation^[7,28,50]. A Chinese expert consensus for the management of diabetes in the elderly^[42] has proposed an overall treatment strategy for management of diabetes in the elderly, including the four principles: (1) early prevention; (2) early diagnosis; (3) early treatment; and (4) early target attainment. Glycemic target management is encouraged to be personalized^[42].

ntidiabetic therapy

The choice of type II diabetes medications has been explicitly suggested in Expert Consensus on Diabetic Diagnosis and Treatments for Elderly^[42]. In brief, first-line antidiabetic therapy includes metformin, α -glucosidase and insulin secretagogues. Metformin has been effective and safe in lowering HbA1c levels. α -glucosidase and insulin secretagogues (glinides and sulfonylurea) are alternatives for older adults who cannot tolerate metformin or who have postprandial

Table 2 Glycemic goals across different clinical conditions of older Chinese (men \geq 45-year-old or women \geq 55-year-old)

Clinical conditions	Glycemic goals
> 10 yr of life expectancy	HbA1c < 7%
Good medical support	Fasting plasma glucose < 7 mmol/L
High expected benefit from treatment	Postprandial blood glucose < 10.0 mmol/L
Low hypoglycaemia risk	Stable blood glucose level
> 10 yr of life expectancy	HbA1c = 7%
New diagnosed and relatively young	
No syndromes or complications	
Low risk of treatment-related hypoglycaemia	
Not using glycaemic-lowering medications or only use one type of non-insulin secretagogues	
Good treatment adherence	
> 10 yr life expectancy	HbA1c < 7.5%
Type I or type II diabetes	
Mild syndromes or complications	
Moderate risk of treatment-related hypoglycaemia	
Receiving insulin secretagogues or insulin therapy	
< 5 yr of life expectancy	HbA1c < 8%
Moderate syndromes or complications	
Moderate risk of hypoglycaemia	
Receiving insulin secretagogues or primarily multiple insulin injections	
< 5 yr of life expectancy	HbA1c < 8.5%
Incapable to self-manage	Avoid acute diabetic complications or refractory infections caused by severe hyperglycaemia
	Blood glucose < 11.1 mmol/L

Table 3 Target levels of blood pressure, low-density lipoprotein cholesterol, non-high-density lipoprotein cholesterol for older Chinese with diabetes

Risk group	Target blood pressure level (mmol/L)	Target lipid level (mmol/L)
Diabetes	< 130/80 mmHg	Primary target LDL-C < 2.6
		Secondary target Non-HDL-C < 3.4
Diabetes with hypertension and another risk factor	< 130/80 mmHg	Primary target LDL-C < 1.8
		Secondary target Non-HDL-C < 2.6

LDL-C: Low-density lipoprotein cholesterol; Non-HDL-C: Non-high-density lipoprotein cholesterol.

hyperglycemia at healthy weights. New diagnosed type 2 diabetic patients who have HbA1c above 9% or FPG above 11.1 mmol/L are recommended to use short-term intensive insulin therapy, including basal and prandial insulin therapy, continuous subcutaneous insulin infusion or premixed insulin for sustaining β -cell function. Chinese patients with type 2 diabetes, who usually have poor early-phase insulin secretion, are recommended to use insulin secretagogues for

lowering blood glucose by stimulating the pancreatic β cell to release insulin. Although sulfonylurea is one of the first-line antidiabetic treatments in China, results of randomized controlled trials on Chinese patients are needed for a better guideline of its use in Chinese patients. Acarbose, a type of α -glucosidase inhibitor, has found to be more effective in lowering postprandial glucose and less useful in fasting plasma glucose than metformin^[51].

Expert Consensus on Diabetic Diagnosis and Treatments for Elderly^[42] also recommended DPP-4 inhibitor and GLP-1 receptor antagonist for treating type 2 diabetes. The effect of DPP4-inhibitors has been as efficacious as acarbose in treating drug-naïve patients with better gastrointestinal tolerability^[52]. Some DPP-4 inhibitors^[53,54] have been associated with improvement of β -cell function in non-Asian patients, but whether such benefit also occurs in Chinese remains unclear. In addition, long-term safety and cardiovascular outcomes of DPP-4 inhibitors in the Chinese population have not been reported^[55].

LIFESTYLE INTERVENTION

Over the past two decades, the industrialization and urbanization of China have fundamentally improved the average standard of living of Chinese; on the other hand, the unhealthy eating patterns and sedentary lifestyles of Chinese have also increased as well^[56]. The China Health and Nutrition Survey (CHNS) reported that the total physical activity and occupational, physical activity in men and women across nine provinces from 1991 to 2011 fell by 31% and 42%, respectively^[57]. Urbanization has been associated with the decreased levels of occupational, physical activities^[58]. Physical inactivity has been associated with increased risks of the five major CVDs in China, including coronary heart disease, stroke, hypertension, type 2 diabetes mellitus and cancer^[59]. Over the past decade, several studies have shown that the food intake patterns of Chinese have dramatically changed as a result of urbanization; grain and vegetables consumptions are decreased, and meat and fats consumption have increased^[56]. The average annual consumption of Chinese adults who were 15 years old or older has gradually increased from 2.5 L in 1978 to 6.7 L in 2010^[60].

Lifestyle modifications such as no smoking, healthy diets, strict alcohol intake and regular exercise, has been suggested by experts and studies worldwide as fundamental part of risk factor management to reduce the risk of CVDs^[1,10,11]. Smoking and second-hand smoking are major risk factors for chronic diseases, including CVD and diabetes^[4,5,9,21,61,62]. They deteriorate the vascular elasticity, accelerate the development of atherosclerosis, and increase the risk of developing CVDs and mortality^[26,63,64]. Therefore, smoking cessation is crucial in reducing the risk of CVDs for both smoking and non-smoking older adults^[10,62]. Effective smoking cessation interventions include

health promotion, nicotine replacement therapy and medication^[65-67].

Salt-sensitive hypertension is common in older adults in China^[4,12,21]; therefore, reduction in salt intake is an essential part of hypertension management strategy^[1,13]. The salt intake of subjects with hypertension is recommended to be < 5 g/d^[21]. Older adults with hypertension are recommended to have high nutritional diets, which include intake of fresh vegetables, fruits, fishes, bean products, coarse grains, skim milk, other rich vitamins, high fiber and non-saturated fats food^[10-12,21]. Of the total calories intake, the proportion of fats and saturated fats consumption are recommended to be less than 25% and 7%, respectively^[21].

Overweight has been associated with risk of elevated blood pressure and lipid levels, and diabetes, which are high-risk factors of CVDs^[68-70]. Modest weight loss has shown improvement in health conditions^[71,72]. In general, the BMI of older adults are encouraged to be under than 25 kg/m²^[21] because the reduction in BMI can alleviate the insulin resistance^[73,74], diabetes^[48,75] and dyslipidemia^[76,77]. Regular moderate exercise can control BMI and insulin resistance, improve systemic cardiovascular modulation and reduce high blood pressure^[78-81]. However, weight-loss medications are in general not recommended to older adults because older adults are susceptible to adverse effects of medications^[10]. Furthermore, excessively strict control of diet and salt intake in older adults often lead to malnutrition^[82-84]. Food consumption is encouraged to be personalized based on individuals' clinical manifestation^[1,12,21]. Rapid or extreme reduction in weight can lead to poor quality of life due to poor physical conditions or even susceptible to develop other systemic diseases^[6,7,12,13,47]. Unlike the younger population, older adults should not have high-intensity exercise because that increases their risk of encountering fracture and fall^[80]. These lifestyles modification factors are highly recommended for management of cardiovascular risk factors, such as obesity, hypertension, dyslipidemia, diabetes and chronic kidney disease^[6,7,69,78,81].

FUTURE PERSPECTIVES

The increasing prevalence of CVD, hypertension, dyslipidemia, and diabetes are increasing in China, but clinical guidelines and expert consensus of primary CVD prevention for older adults or very old adults are currently lacking. Unlike management of a particular risk factor (e.g., hypertension, dyslipidemia) which considers treatment strategies that optimize a specific factor, primary CVD prevention strategies require treatment plans that simultaneously manage several risk factors. A systematic review in 2016 reported that many primary CVD preventions of clinical practice guidelines (CPGs) in other countries have inexplicit guidance to manage CVD risk factors of older adults^[11]. Although that systematic review only reviewed English

articles, some limitations that were revealed in that review also applied to Chinese clinical guidelines and expert consensus of primary CVD prevention in older adults and very old adults: (1) limited discussion of primary prevention strategies for frail older people and older individuals with multiple comorbidities; (2) no recommendations on how to overcome problems that withhold the implementation of the CPG for older people such as treatment adherence; and (3) no specific guidance on how to prioritize treatments with consideration of multiple comorbidities, personal and family preferences, and vulnerability to adverse drug effects.

The development of CPG is recommended to be structured in ways that clearly outline primary CVD strategies for a wide variety of older Chinese. In addition, CPGs are recommended to include specific guidance to guide clinicians how to develop personalized primary CVD prevention strategies that take into consideration of clinical manifestations, tolerability, and multiple comorbidities.

In addition, with the increasing prevalence of diabetes, hypertension and dyslipidemia in Chinese elderly, better management of risk factors of CVDs for this growing population are needed. Better management of CVD risk factors includes additional research on optimizing the use of medications in the elderly and safer methods of administering medications to avoid treatment-related adverse outcomes. Personalize, analyze, and dynamically adjust treatment plans according to responses from patients are crucial as well. The awareness and treatments of hypertension, dyslipidemia, and diabetes remain low^[4,14,50,85-87]; hence, more education and training and additional social services are also encouraged in China.

Multi-center large randomized trials of primary CVD prevention on older people (with the inclusion of the frail older people with comorbidities) in China are recommended to explore optimal treatment strategies and targets of blood pressure for older adults in China. Large double-blinded randomized controlled trials on very old people (age > 80 years old) are needed to assess the lipid-lowering effect and adverse effect of statin therapies and some non-statin therapies (Omega-3 fatty acid and bile acid sequestrants) on older adults with multiple comorbidities. More studies are needed to assess the antihypertensive effect of carvedilol and nebivolol and the long-term safety of DPP-4 inhibitors on Chinese elderly. Furthermore, additional studies are needed to evaluate the benefit and harm of lowering blood pressure targets of diabetic older patients to be under 130/80 mmHg^[12,21]. The implementation of these suggestions may remarkably reduce the risk of CVDs in older adults *via* more effective management of CVD-related risk factors.

CONCLUSION

In China, CVD has been the leading cause of death,

and the percentage of Chinese who are 60 years or older are increasing. Prescribing cardiovascular treatments to older adults are usually more challenging than younger adults due to polypharmacy, the presence of comorbidities and more susceptible to treatment-related adverse outcomes. Therefore, primary prevention of CVD for older adults is crucial to sustaining the health of older adults and reducing health care burden. Risks of CVDs in older adults can be remarkably reduced through appropriate management of CVD-related risk factors, such as hypertension, dyslipidemia, diabetes and obesity, by controlling blood pressure, glucose and lipids through lifestyle modifications or receiving medications. Lifestyle modifications such as smoking cessation, healthy diets, strict alcohol intake and moderate physical exercise have been recommended to effectively improve health conditions of older adults who have hypertension, dyslipidemia, obesity, diabetes or complications. Treatments for older adults, in general, are recommended to be personalized and to be initiated at low doses. The future direction for better primary CVD prevention in older adults include establishing guidelines for primary prevention of CVD across diverse older adults and further research on better management of CVD risks for elderly Chinese.

REFERENCES

- 1 **Chinese Society of Cardiology of Chinese Medical Association, Editorial Board of Chinese Journal of Cardiology.** [Chinese guidelines for prevention of cardiovascular diseases]. *Zhonghua Xin Xue Guan Bing Za Zhi* 2011; **39**: 3-22 [PMID: 21418789 DOI: 10.3760/cma.j.issn.0253-3758.2011.01.002]
- 2 **Zhou M,** Wang H, Zhu J, Chen W, Wang L, Liu S, Li Y, Wang L, Liu Y, Yin P, Liu J, Yu S, Tan F, Barber RM, Coates MM, Dicker D, Fraser M, González-Medina D, Hamavid H, Hao Y, Hu G, Jiang G, Kan H, Lopez AD, Phillips MR, She J, Vos T, Wan X, Xu G, Yan LL, Yu C, Zhao Y, Zheng Y, Zou X, Naghavi M, Wang Y, Murray CJ, Yang G, Liang X. Cause-specific mortality for 240 causes in China during 1990-2013: a systematic subnational analysis for the Global Burden of Disease Study 2013. *Lancet* 2016; **387**: 251-272 [PMID: 26510778 DOI: 10.1016/s0140-6736(15)00551-6]
- 3 China statistical year book 2016. Beijing, China: National Bureau of Statistics of China, 2016
- 4 **Chen WW,** Gao RL, Liu LS, Zhu ML, Wang W, Wang YJ, Wu ZS, Li HJ, Gu DF, Yang YJ, Zheng Z, Jiang LX, Hu SS. China cardiovascular diseases report 2015: a summary. *J Geriatr Cardiol* 2017; **14**: 1-10 [PMID: 28270835 DOI: 10.11909/j.issn.1671-5411.2017.01.012]
- 5 **Aronow WS.** Blood Pressure Goals and Targets in the Elderly. *Curr Treat Options Cardiovasc Med* 2015; **17**: 394 [PMID: 26081967 DOI: 10.1007/s11936-015-0394-x]
- 6 **Ye P.** Management for dyslipidemia in the elderly. *Chin J Mult Organ Dis Elderly* 2015; **14**: 569-572 [DOI: 10.11915/j.issn.1671-5403.2015.08.130]
- 7 **Bansal N,** Dhaliwal R, Weinstock RS. Management of diabetes in the elderly. *Med Clin North Am* 2015; **99**: 351-377 [PMID: 25700588 DOI: 10.1016/j.mcna.2014.11.008]
- 8 **Stevens W,** Peneva D, Li JZ, Liu LZ, Liu G, Gao R, Lakdawalla DN. Estimating the future burden of cardiovascular disease and the value of lipid and blood pressure control therapies in China. *BMC Health Serv Res* 2016; **16**: 175 [PMID: 27165638 DOI: 10.1186/s12913-016-1420-8]
- 9 **Wu Y,** Benjamin EJ, MacMahon S. Prevention and Control of Cardiovascular Disease in the Rapidly Changing Economy of China. *Circulation* 2016; **133**: 2545-2560 [PMID: 27297347 DOI: 10.1161/circulationaha.115.008728]
- 10 **Aronow CN.** Primary prevention of cardiovascular disease: new guidelines, technologies and therapies. *Med J Aust* 2014; **200**: 146-147 [PMID: 24528420 DOI: 10.5694/mja13.11084]
- 11 **Jansen J,** McKinn S, Bonner C, Irwig L, Doust J, Glasziou P, Nickel B, van Munster B, McCaffery K. Systematic review of clinical practice guidelines recommendations about primary cardiovascular disease prevention for older adults. *BMC Fam Pract* 2015; **16**: 104 [PMID: 26289559 DOI: 10.1186/s12875-015-0310-1]
- 12 **Hypertension Branch of Chinese Geriatric Medical Association.** China experts consensus on the managements of hypertension in the very old people. *Chin J Cardiovas Med* 2015; **20**: 401-409 [DOI: 10.3969/j.issn.1007-5410.2015.06.001]
- 13 **Chinese Society of Neurology,** Cerebrovascular Disease Group of Chinese Society of Neurology. Chinese primary cerebrovascular disease prevention guidelines 2015. *Chin J Neurol* 2015; **48**: 629-643 [DOI: 10.3760/cma.j.issn.1006-7876.2015.08.003]
- 14 **Wu J,** Cheng X, Qiu L, Xu T, Zhu G, Han J, Xia L, Qin X, Cheng Q, Liu Q. Prevalence and Clustering of Major Cardiovascular Risk Factors in China: A Recent Cross-Sectional Survey. *Medicine (Baltimore)* 2016; **95**: e2712 [PMID: 26962771 DOI: 10.1097/MD.0000000000002712]
- 15 **Ji L,** Hu D, Pan C, Weng J, Huo Y, Ma C, Mu Y, Hao C, Ji Q, Ran X, Su B, Zhuo H, Fox KA, Weber M, Zhang D; CCMR Advisory Board; CCMR-3B STUDY Investigators. Primacy of the 3B approach to control risk factors for cardiovascular disease in type 2 diabetes patients. *Am J Med* 2013; **126**: 925.e11-925.e22 [PMID: 23810406 DOI: 10.1016/j.amjmed.2013.02.035]
- 16 **Beckett NS,** Peters R, Fletcher AE, Staessen JA, Liu L, Dumitrascu D, Stoyanovsky V, Antikainen RL, Nikitin Y, Anderson C, Belhani A, Forette F, Rajkumar C, Thijs L, Banya W, Bulpitt CJ; HYVET Study Group. Treatment of hypertension in patients 80 years of age or older. *N Engl J Med* 2008; **358**: 1887-1898 [PMID: 18378519 DOI: 10.1056/NEJMoa0801369]
- 17 **Bundy JD,** He J. Hypertension and Related Cardiovascular Disease Burden in China. *Ann Glob Health* 2016; **82**: 227-233 [PMID: 27372527 DOI: 10.1016/j.aogh.2016.02.002]
- 18 **Chalmers J,** MacMahon S, Mancia G, Whitworth J, Beilin L, Hansson L, Neal B, Rodgers A, Ni Mhurchu C, Clark T. 1999 World Health Organization-International Society of Hypertension Guidelines for the management of hypertension. Guidelines subcommittee of the World Health Organization. *Clin Exp Hypertens* 1999; **21**: 1009-1060 [PMID: 10423121 DOI: 10.3109/10641969909061028]
- 19 **Buford TW.** Hypertension and aging. *Ageing Res Rev* 2016; **26**: 96-111 [PMID: 26835847 DOI: 10.1016/j.arr.2016.01.007]
- 20 **Lewington S,** Lacey B, Clarke R, Guo Y, Kong XL, Yang L, Chen Y, Bian Z, Chen J, Meng J, Xiong Y, He T, Pang Z, Zhang S, Collins R, Peto R, Li L, Chen Z; China Kadoorie Biobank Consortium. The Burden of Hypertension and Associated Risk for Cardiovascular Mortality in China. *JAMA Intern Med* 2016; **176**: 524-532 [PMID: 26975032 DOI: 10.1001/jamainternmed.2016.0190]
- 21 **Chinese Society of Cardiology,** China Association of Gerontology and Geriatrics. Chinese expert consensus on the diagnosis and treatment of hypertension in the elderly (2011 version). *Chin J Intern Med* 2012; **51**: 76-82 [DOI: 10.3760/cma.j.issn.0578-1426.2012.01.023]
- 22 **Pimenta E,** Oparil S. Management of hypertension in the elderly. *Nat Rev Cardiol* 2012; **9**: 286-296 [PMID: 22411292 DOI: 10.1038/nrcardio.2012.27]
- 23 **Bangalore S,** Messerli FH, Wun CC, Zuckerman AL, DeMicco D, Kostis JB, LaRosa JC; Treating to New Targets Steering Committee and Investigators. J-curve revisited: An analysis of blood pressure and cardiovascular events in the Treating to New Targets (TNT) Trial. *Eur Heart J* 2010; **31**: 2897-2908 [PMID: 20846991 DOI: 10.1093/eurheartj/ehq328]

- 24 **Verdecchia P**, Angeli F, Mazzotta G, Garofoli M, Reboldi G. Aggressive blood pressure lowering is dangerous: the J-curve: con side of the argument. *Hypertension* 2014; **63**: 37-40 [PMID: 24336630 DOI: 10.1161/01.hyp.0000439102.43479.43]
- 25 **Farnett L**, Mulrow CD, Linn WD, Lucey CR, Tuley MR. The J-curve phenomenon and the treatment of hypertension. Is there a point beyond which pressure reduction is dangerous? *JAMA* 1991; **265**: 489-495 [PMID: 1824642 DOI: 10.1001/jama.1991.03460040065031]
- 26 **Wang Y**, Qi F, Jia X, Lin P, Liu H, Geng M, Liu Y, Li S, Tan J. Mortality and Burden of Disease Attributable to Cigarette Smoking in Qingdao, China. *Int J Environ Res Public Health* 2016; **13**: 898-897 [PMID: 27618084 DOI: 10.3390/ijerph13090898]
- 27 **Lonsdale DO**, Baker EH. Understanding and managing medication in elderly people. *Best Pract Res Clin Obstet Gynaecol* 2013; **27**: 767-788 [PMID: 23850054 DOI: 10.1016/j.bpobgyn.2013.06.002]
- 28 **Araki A**, Ito H. Diabetes mellitus and geriatric syndromes. *Geriatr Gerontol Int* 2009; **9**: 105-114 [PMID: 19740352 DOI: 10.1111/j.1447-0594.2008.00495.x]
- 29 **Roush GC**, Sica DA. Diuretics for Hypertension: A Review and Update. *Am J Hypertens* 2016; **29**: 1130-1137 [PMID: 27048970 DOI: 10.1093/ajh/hpw030]
- 30 **Chen GY**, Li L, Dai F, Li XJ, Xu XX, Fan JG. Prevalence of and Risk Factors for Type 2 Diabetes Mellitus in Hyperlipidemia in China. *Med Sci Monit* 2015; **21**: 2476-2484 [PMID: 26297334 DOI: 10.12659/MSM.894246]
- 31 **Pan L**, Yang Z, Wu Y, Yin RX, Liao Y, Wang J, Gao B, Zhang L; China National Survey of Chronic Kidney Disease Working Group. The prevalence, awareness, treatment and control of dyslipidemia among adults in China. *Atherosclerosis* 2016; **248**: 2-9 [PMID: 26978581 DOI: 10.1016/j.atherosclerosis.2016.02.006]
- 32 **Stone NJ**, Robinson JG, Lichtenstein AH, Bairey Merz CN, Blum CB, Eckel RH, Goldberg AC, Gordon D, Levy D, Lloyd-Jones DM, McBride P, Schwartz JS, Shero ST, Smith SC Jr, Watson K, Wilson PW; American College of Cardiology/American Heart Association Task Force on Practice Guidelines. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol* 2014; **63**: 2889-2934 [PMID: 24239923 DOI: 10.1016/j.jacc.2013.11.002]
- 33 **Catapano AL**, Graham I, De Backer G, Wiklund O, Chapman MJ, Drexel H, Hoes AW, Jennings CS, Landmesser U, Pedersen TR, Reiner Z, Riccardi G, Taskinen MR, Tokgozoglu L, Verschuren WM, Vlachopoulos C, Wood DA, Zamorano JL. 2016 ESC/EAS Guidelines for the Management of Dyslipidaemias: The Task Force for the Management of Dyslipidaemias of the European Society of Cardiology (ESC) and European Atherosclerosis Society (EAS) Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR). *Atherosclerosis* 2016; **253**: 281-344 [PMID: 27594540 DOI: 10.1093/eurheartj/ehw272]
- 34 **Joint committee issued Chinese guideline for the management of dyslipidemia in adults**. [2016 Chinese guideline for the management of dyslipidemia in adults]. *Zhonghua Xin Xue Guan Bing Za Zhi* 2016; **44**: 833-853 [PMID: 27903370 DOI: 10.3760/cma.j.issn.0253-3758.2016.10.005]
- 35 **Reiner Z**. Primary prevention of cardiovascular disease with statins in the elderly. *Curr Atheroscler Rep* 2014; **16**: 420 [PMID: 24781597 DOI: 10.1007/s11883-014-0420-6]
- 36 **Teng M**, Lin L, Zhao YJ, Khoo AL, Davis BR, Yong QW, Yeo TC, Lim BP. Statins for Primary Prevention of Cardiovascular Disease in Elderly Patients: Systematic Review and Meta-Analysis. *Drugs Aging* 2015; **32**: 649-661 [PMID: 26245770 DOI: 10.1007/s40266-015-0290-9]
- 37 **Lonn EM**, Bosch J, López-Jaramillo P, Zhu J, Liu L, Pais P, Diaz R, Xavier D, Sliwa K, Dans A, Avezum A, Piegas LS, Keltai K, Keltai M, Chazova I, Peters RJ, Held C, Yusuf K, Lewis BS, Jansky P, Parkhomenko A, Khunti K, Toff WD, Reid CM, Varigos J, Leiter LA, Molina DI, McKelvie R, Pogue J, Wilkinson J, Jung H, Dagenais G, Yusuf S; HOPE-3 Investigators. Blood-Pressure Lowering in Intermediate-Risk Persons without Cardiovascular Disease. *N Engl J Med* 2016; **374**: 2009-2020 [PMID: 27041480 DOI: 10.1056/NEJMoa1600175]
- 38 **Koren MJ**, Giugliano RP, Raal FJ, Sullivan D, Bolognese M, Langslet G, Civeira F, Somaratne R, Nelson P, Liu T, Scott R, Wasserman SM, Sabatine MS; OSLER Investigators. Efficacy and safety of longer-term administration of evolocumab (AMG 145) in patients with hypercholesterolemia: 52-week results from the Open-Label Study of Long-Term Evaluation Against LDL-C (OSLER) randomized trial. *Circulation* 2014; **129**: 234-243 [PMID: 24255061 DOI: 10.1161/circulationaha.113.007012]
- 39 **Watts GF**, Stefanutti C. ODYSSEY ESCAPE: is PCSK9 inhibition the Trojan Horse for the use of lipoprotein apheresis in familial hypercholesterolaemia? *Eur Heart J* 2016; **37**: 3596-3599 [PMID: 28087751 DOI: 10.1093/eurheartj/ehw497]
- 40 **Savarese G**, Gotto AM Jr, Paolillo S, D'Amore C, Losco T, Musella F, Scala O, Marciano C, Ruggiero D, Marsico F, De Luca G, Trimarco B, Perrone-Filardi P. Benefits of statins in elderly subjects without established cardiovascular disease: a meta-analysis. *J Am Coll Cardiol* 2013; **62**: 2090-2099 [PMID: 23954343 DOI: 10.1016/j.jacc.2013.07.069]
- 41 **HPS2-THRIVE Collaborative Group**. HPS2-THRIVE randomized placebo-controlled trial in 25 673 high-risk patients of ER niacin/laropiprant: trial design, pre-specified muscle and liver outcomes, and reasons for stopping study treatment. *Eur Heart J* 2013; **34**: 1279-1291 [PMID: 23444397 DOI: 10.1093/eurheartj/ehs055]
- 42 **Geriatric Endocrinological Committee of China Association of Gerontology**, Expert Consensus Writing Group of Geriatric Diabetic Treatments and Diagnosis. Expert consensus on diabetic diagnosis and treatments for elderly (2013). *Chin J Intern Med* 2014; **53**: 243-251 [DOI: 10.3760/cma.j.issn.0578-1426.2014.03.027]
- 43 **Expert Dyslipidemia Panel of the International Atherosclerosis Society Panel members**. An International Atherosclerosis Society Position Paper: global recommendations for the management of dyslipidemia--full report. *J Clin Lipidol* 2014; **8**: 29-60 [PMID: 24528685 DOI: 10.1016/j.jacl.2013.12.005]
- 44 **Dixon DL**, Donohoe KL, Ogbonna KC, Barden SM. Current drug treatment of hyperlipidemia in older adults. *Drugs Aging* 2015; **32**: 127-138 [PMID: 25637391 DOI: 10.1007/s40266-015-0240-6]
- 45 **Tuomi T**, Santoro N, Caprio S, Cai M, Weng J, Groop L. The many faces of diabetes: a disease with increasing heterogeneity. *Lancet* 2014; **383**: 1084-1094 [PMID: 24315621 DOI: 10.1016/s0140-6736(13)62219-9]
- 46 **World Health Organization**. Obesity: preventing and managing the global epidemic. Report of a WHO consultation. *World Health Organ Tech Rep Ser* 2000; **894**: i-xii, 1-253 [PMID: 11234459 DOI: 10.1017/S0021932003245508]
- 47 **China Expert Consensus Group of Statins on Elderly with Dyslipidemia**. Chinese experts consensus on the use of statins on elderly with dyslipidemia. *Chin J Cardiovas Med* 2015; **54**: 467-477 [DOI: 10.3760/cma.j.issn.0578-1426.2015.05.020]
- 48 **Channanath AM**, Farran B, Behbehani K, Thanaraj TA. Association between body mass index and onset of hypertension in men and women with and without diabetes: a cross-sectional study using national health data from the State of Kuwait in the Arabian Peninsula. *BMJ Open* 2015; **5**: e007043 [PMID: 26044759 DOI: 10.1136/bmjopen-2014-007043]
- 49 **Epidemiology Group of Chinese Cardiology Society of Chinese Medical Association**, Cardiovascular Internal Medicine Society of Chinese Medical Association, Chinese Association of Gerontology and Geriatrics. Clinical diagnosis and treatments guidelines of glycemic metabolism disorder and atherosclerotic cardiovascular disease. *Chin J Cardiology* 2015; **43**: 488-506 [DOI: 10.3760/cma.j.issn.0253-3758.2015.06.008]
- 50 **Zhao Y**, Crimmins EM, Hu P, Shen Y, Smith JP, Strauss J, Wang Y, Zhang Y. Prevalence, diagnosis, and management of diabetes mellitus among older Chinese: results from the China Health and Retirement Longitudinal Study. *Int J Public Health* 2016; **61**: 347-356 [PMID: 26755457 DOI: 10.1007/s00038-015-0780-x]

- 51 **Yang W**, Liu J, Shan Z, Tian H, Zhou Z, Ji Q, Weng J, Jia W, Lu J, Liu J, Xu Y, Yang Z, Chen W. Acarbose compared with metformin as initial therapy in patients with newly diagnosed type 2 diabetes: an open-label, non-inferiority randomised trial. *Lancet Diabetes Endocrinol* 2014; **2**: 46-55 [PMID: 24622668 DOI: 10.1016/S2213-8587(13)70021-4]
- 52 **Pan C**, Yang W, Barona JP, Wang Y, Niggli M, Mohideen P, Wang Y, Foley JE. Comparison of vildagliptin and acarbose monotherapy in patients with Type 2 diabetes: a 24-week, double-blind, randomized trial. *Diabet Med* 2008; **25**: 435-441 [PMID: 18341596 DOI: 10.1111/j.1464-5491.2008.02391.x]
- 53 **Goldstein BJ**, Feinglos MN, Lunceford JK, Johnson J, Williams-Herman DE; Sitagliptin 036 Study Group. Effect of initial combination therapy with sitagliptin, a dipeptidyl peptidase-4 inhibitor, and metformin on glycemic control in patients with type 2 diabetes. *Diabetes Care* 2007; **30**: 1979-1987 [PMID: 17485570 DOI: 10.2337/dc07-0627]
- 54 **Rosenstock J**, Aguilar-Salinas C, Klein E, Nepal S, List J, Chen R; CV181-011 Study Investigators. Effect of saxagliptin monotherapy in treatment-naïve patients with type 2 diabetes. *Curr Med Res Opin* 2009; **25**: 2401-2411 [PMID: 19650754 DOI: 10.1185/03007990903178735]
- 55 **Yang W**, Weng J. Early therapy for type 2 diabetes in China. *Lancet Diabetes Endocrinol* 2014; **2**: 992-1002 [PMID: 25218729 DOI: 10.1016/S2213-8587(14)70136-6]
- 56 **Gong P**, Liang S, Carlton EJ, Jiang Q, Wu J, Wang L, Remais JV. Urbanisation and health in China. *Lancet* 2012; **379**: 843-852 [PMID: 22386037 DOI: 10.1016/S0140-6736(11)61878-3]
- 57 **Ng SW**, Howard AG, Wang HJ, Su C, Zhang B. The physical activity transition among adults in China: 1991-2011. *Obes Rev* 2014; **15** Suppl 1: 27-36 [PMID: 24341756 DOI: 10.1111/obr.12127]
- 58 **Ng SW**, Norton EC, Popkin BM. Why have physical activity levels declined among Chinese adults? Findings from the 1991-2006 China Health and Nutrition Surveys. *Soc Sci Med* 2009; **68**: 1305-1314 [PMID: 19232811 DOI: 10.1016/j.socscimed.2009.01.035]
- 59 **Zhang J**, Chaaban J. The economic cost of physical inactivity in China. *Prev Med* 2013; **56**: 75-78 [PMID: 23200874 DOI: 10.1016/j.ypmed.2012.11.010]
- 60 **Jiang H**, Room R, Hao W. Alcohol and related health issues in China: action needed. *Lancet Glob Health* 2015; **3**: e190-e191 [PMID: 25794669 DOI: 10.1016/S2214-109X(15)70017-3]
- 61 **Pan A**, Wang Y, Talaei M, Hu FB. Relation of Smoking With Total Mortality and Cardiovascular Events Among Patients With Diabetes Mellitus: A Meta-Analysis and Systematic Review. *Circulation* 2015; **132**: 1795-1804 [PMID: 26311724 DOI: 10.1161/circulationaha.115.017926]
- 62 **Xu X**, Liu L, Sharma M, Zhao Y. Smoking-related knowledge, attitudes, behaviors, smoking cessation idea and education level among young adult male smokers in Chongqing, China. *Int J Environ Res Public Health* 2015; **12**: 2135-2149 [PMID: 25689992 DOI: 10.3390/ijerph120202135]
- 63 **Zheng W**, McLerran DF, Rolland BA, Fu Z, Boffetta P, He J, Gupta PC, Ramadas K, Tsugane S, Irie F, Tamakoshi A, Gao YT, Koh WP, Shu XO, Ozasa K, Nishino Y, Tsuji I, Tanaka H, Chen CJ, Yuan JM, Ahn YO, Yoo KY, Ahsan H, Pan WH, Qiao YL, Gu D, Pednekar MS, Sauvaget C, Sawada N, Sairenchi T, Yang G, Wang R, Xiang YB, Ohishi W, Kakizaki M, Watanabe T, Oze I, You SL, Sugawara Y, Butler LM, Kim DH, Park SK, Parvez F, Chuang SY, Fan JH, Shen CY, Chen Y, Grant EJ, Lee JE, Sinha R, Matsuo K, Thornquist M, Inoue M, Feng Z, Kang D, Potter JD. Burden of total and cause-specific mortality related to tobacco smoking among adults aged ≥ 45 years in Asia: a pooled analysis of 21 cohorts. *PLoS Med* 2014; **11**: e1001631 [PMID: 24756146 DOI: 10.1371/journal.pmed.1001631]
- 64 **Lv J**, Chen W, Sun D, Li S, Millwood IY, Smith M, Guo Y, Bian Z, Yu C, Zhou H, Tan Y, Chen J, Chen Z, Li L; China Kadoorie Biobank collaborative group. Gender-specific association between tobacco smoking and central obesity among 0.5 million Chinese people: the China Kadoorie Biobank Study. *PLoS One* 2015; **10**: e0124586 [PMID: 25897789 DOI: 10.1371/journal.pone.0124586]
- 65 **Hughes JR**, Stead LF, Hartmann-Boyce J, Cahill K, Lancaster T. Antidepressants for smoking cessation. *Cochrane Database Syst Rev* 2014; **(1)**: CD000031 [PMID: 24402784 DOI: 10.1002/14651858.CD000031.pub4]
- 66 **Stead LF**, Perera R, Bullen C, Mant D, Hartmann-Boyce J, Cahill K, Lancaster T. Nicotine replacement therapy for smoking cessation. *Cochrane Database Syst Rev* 2012; **11**: CD000146 [PMID: 23152200 DOI: 10.1002/14651858.cd000146]
- 67 **Stead LF**, Buitrago D, Preciado N, Sanchez G, Hartmann-Boyce J, Lancaster T. Physician advice for smoking cessation. *Cochrane Database Syst Rev* 2013; **(5)**: CD000165 [PMID: 23728631 DOI: 10.1002/14651858.cd000165.pub4]
- 68 **Qi SF**, Zhang B, Wang HJ, Yan J, Du P, Zhang W, Mi YJ, Zhao JJ, Liu DW, Tian QB. Joint effects of age and body mass index on the incidence of hypertension subtypes in the China Health and Nutrition Survey: A cohort study over 22years. *Prev Med* 2016; **89**: 23-30 [PMID: 27155441 DOI: 10.1016/j.ypmed.2016.05.004]
- 69 **Hall ME**, do Carmo JM, da Silva AA, Juncos LA, Wang Z, Hall JE. Obesity, hypertension, and chronic kidney disease. *Int J Nephrol Renovasc Dis* 2014; **7**: 75-88 [PMID: 24600241 DOI: 10.2147/ijnrd.s39739]
- 70 **Stiefel EC**, Field L, Replogle W, McIntyre L, Igboechi O, Savoie FH 3rd. The Prevalence of Obesity and Elevated Blood Pressure in Adolescent Student Athletes From the State of Mississippi. *Orthop J Sports Med* 2016; **4**: 2325967116629368 [PMID: 26962540 DOI: 10.1177/2325967116629368]
- 71 **Gudzune KA**, Doshi RS, Mehta AK, Chaudhry ZW, Jacobs DK, Vakil RM, Lee CJ, Bleich SN, Clark JM. Efficacy of commercial weight-loss programs: an updated systematic review. *Ann Intern Med* 2015; **162**: 501-512 [PMID: 25844997 DOI: 10.7326/m14-2238]
- 72 **Swift DL**, Johannsen NM, Lavie CJ, Earnest CP, Church TS. The role of exercise and physical activity in weight loss and maintenance. *Prog Cardiovasc Dis* 2014; **56**: 441-447 [PMID: 24438736 DOI: 10.1016/j.pcad.2013.09.012]
- 73 **Lee BC**, Lee J. Cellular and molecular players in adipose tissue inflammation in the development of obesity-induced insulin resistance. *Biochim Biophys Acta* 2014; **1842**: 446-462 [PMID: 23707515 DOI: 10.1016/j.bbdis.2013.05.017]
- 74 **Gandhe MB**, M L, Srinivasan AR. Evaluation of Body Mass Index (BMI) Percentile cut-off Levels with Reference to Insulin Resistance: A Comparative Study on South Indian Obese and Non-Obese Adolescents. *J Clin Diagn Res* 2013; **7**: 1579-1582 [PMID: 24086844 DOI: 10.7860/jcdr/2013/6263.3213]
- 75 **Araneta MR**, Kanaya AM, Hsu WC, Chang HK, Grandinetti A, Boyko EJ, Hayashi T, Kahn SE, Leonetti DL, McNeely MJ, Onishi Y, Sato KK, Fujimoto WY. Optimum BMI cut points to screen asian americans for type 2 diabetes. *Diabetes Care* 2015; **38**: 814-820 [PMID: 25665815 DOI: 10.2337/dc14-2071]
- 76 **Feng RN**, Zhao C, Wang C, Niu YC, Li K, Guo FC, Li ST, Sun CH, Li Y. BMI is strongly associated with hypertension, and waist circumference is strongly associated with type 2 diabetes and dyslipidemia, in northern Chinese adults. *J Epidemiol* 2012; **22**: 317-323 [PMID: 22672914 DOI: 10.2188/jea.JE20110120]
- 77 **Zhu Y**, Shao Z, Jing J, Ma J, Chen Y, Li X, Yang W, Guo L, Jin Y. Body Mass Index Is Better than Other Anthropometric Indices for Identifying Dyslipidemia in Chinese Children with Obesity. *PLoS One* 2016; **11**: e0149392 [PMID: 26963377 DOI: 10.1371/journal.pone.0149392]
- 78 **Lavie CJ**, Thomas RJ, Squires RW, Allison TG, Milani RV. Exercise training and cardiac rehabilitation in primary and secondary prevention of coronary heart disease. *Mayo Clin Proc* 2009; **84**: 373-383 [PMID: 19339657 DOI: 10.1016/S0025-6196(11)60548-X]
- 79 **Britton KA**, Mukamal KJ, Ix JH, Siscovick DS, Newman AB, de Boer IH, Thacker EL, Biggs ML, Gaziano JM, Djoussé L. Insulin resistance and incident peripheral artery disease in the Cardiovascular Health Study. *Vasc Med* 2012; **17**: 85-93 [PMID: 22402937 DOI: 10.1177/1358863x11436195]
- 80 **Buchner DM**. Physical activity and prevention of cardiovascular

- disease in older adults. *Clin Geriatr Med* 2009; **25**: 661-675, viii [PMID: 19944266 DOI: 10.1016/j.cger.2009.08.002]
- 81 **Soares-Miranda L**, Siscovick DS, Psaty BM, Longstreth WT Jr, Mozaffarian D. Physical Activity and Risk of Coronary Heart Disease and Stroke in Older Adults: The Cardiovascular Health Study. *Circulation* 2016; **133**: 147-155 [PMID: 26538582 DOI: 10.1161/circulationaha.115.018323]
 - 82 **Singh DK**, Manaf ZA, Yusoff NA, Muhammad NA, Phan MF, Shahar S. Correlation between nutritional status and comprehensive physical performance measures among older adults with undernourishment in residential institutions. *Clin Interv Aging* 2014; **9**: 1415-1423 [PMID: 25187701 DOI: 10.2147/cia.s64997]
 - 83 **Deierlein AL**, Morland KB, Scanlin K, Wong S, Spark A. Diet quality of urban older adults age 60 to 99 years: the Cardiovascular Health of Seniors and Built Environment Study. *J Acad Nutr Diet* 2014; **114**: 279-287 [PMID: 24262516 DOI: 10.1016/j.jand.2013.09.002]
 - 84 **Porter Starr KN**, McDonald SR, Bales CW. Nutritional Vulnerability in Older Adults: A Continuum of Concerns. *Curr Nutr Rep* 2015; **4**: 176-184 [PMID: 26042189 DOI: 10.1007/s13668-015-0118-6]
 - 85 **Xu S**, Ming J, Xing Y, Jia A, Cai J, Jing C, Ji Q; China National Diabetes and Metabolic Disorders Study Group. Diabetes awareness and screening in high-risk populations in China: A nationwide, population-based survey. *Lancet Diabetes Endocrinol* 2016; **4** Suppl 1: S27 [DOI: 10.1016/S2213-8587(16)30382-5]
 - 86 **Xu Y**, Wang L, He J, Bi Y, Li M, Wang T, Wang L, Jiang Y, Dai M, Lu J, Xu M, Li Y, Hu N, Li J, Mi S, Chen CS, Li G, Mu Y, Zhao J, Kong L, Chen J, Lai S, Wang W, Zhao W, Ning G; 2010 China Noncommunicable Disease Surveillance Group. Prevalence and control of diabetes in Chinese adults. *JAMA* 2013; **310**: 948-959 [PMID: 24002281 DOI: 10.1001/jama.2013.168118]
 - 87 **Song L**, Shen L, Li H, Liu B, Zheng X, Liang Y, Yuan J, Wang Y. Height and prevalence of hypertension in a middle-aged and older Chinese population. *Sci Rep* 2016; **6**: 39480 [PMID: 28000763 DOI: 10.1038/srep39480]

P- Reviewer: Chello M, De Maria E **S- Editor:** Ji FF **L- Editor:** A
E- Editor: Zhao LM





Published by **Baishideng Publishing Group Inc**
7901 Stoneridge Drive, Suite 501, Pleasanton, CA 94588, USA
Telephone: +1-925-223-8242
Fax: +1-925-223-8243
E-mail: bpgoffice@wjgnet.com
Help Desk: <http://www.f6publishing.com/helpdesk>
<http://www.wjgnet.com>

