The effectiveness of Dietary Approaches to Stop Hypertension (DASH) counselling on estimated 10-year cardiovascular risk among patients with newly diagnosed grade 1 hypertension: a randomised clinical trial

Martin CS Wong, MD [a]; Harry HX Wang, PhD [b, c,]*; Mandy WM Kwan, MSc [a, d]; Shannon TS Li, MPH [a]; Miaoyin Liang, MPH [a]; Franklin TH Fung, BHSc [a]; Ming Sze Yeung, BSc [a]; Brian CY Fong, MPH [a, e]; De Xing Zhang, PhD [a]; David KL Chan, BSc [a]; Bryan P Yan, FRACP, FESC, FACC [f]; Andrew JS Coats, FRCP, FRACP, FESC [f, g, h]; Sian M Griffiths, FFPH, FRCP [a]

[a] JC School of Public Health and Primary Care, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong

[b] School of Public Health, Sun Yat-Sen University, Guangzhou 510080, P.R. China

[c] General Practice and Primary Care, Institute of Health and Wellbeing, University of Glasgow, Glasgow G12 9LX, UK

[d] Department of Family Medicine, Hospital Authority, Hong Kong

[e] Department of Health, The Government of the Hong Kong Special Administrative Region, Hong Kong

[f] Department of Medicine and Therapeutics, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong

[g] Monash University, Australia

[h] The University of Warwick, UK

Running Title: DASH counselling on cardiovascular risk

Grant Support: Health and Medical Research Fund, Hong Kong Government

Disclosures: None declared

Key words: Dietary Approaches to Stop Hypertension (DASH); cardiovascular risk; dietary counselling; associated factors; primary care

***Corresponding author:** Harry HX Wang BS, MS, PhD

School of Public Health, Sun Yat-Sen University, No.74 Zhongshan Road 2, Guangzhou 510080, P.R. China; JC School of Public Health and Primary Care, The Chinese University of Hong Kong, Shatin, NT., Hong Kong; General Practice and Primary Care, Institute of Health and Wellbeing, University of Glasgow, 1 Horselethill Road, Glasgow G12 9LX, UK

Tel: +852 2252 8784; **E-mail:** haoxiangwang@163.com; Haoxiang.Wang@glasgow.ac.uk

Abstract

Background: The Dietary Approaches to Stop Hypertension (DASH) has been shown to lower blood pressure in the West. However, the real-life impact of DASH on reducing cardiovascular (CV) risk in routine clinical setting has not been studied.

Methods: A parallel-group, open-labelled, physician-blinded, randomised controlled trial was conducted in January-June 2013 and followed up for 6- and 12-months in primary care settings in Hong Kong. Patients newly diagnosed with grade 1 hypertension (aged 40-70 years) who had no concomitant medical conditions requiring dietary modifications were consecutively recruited. Subjects were randomised to standard education (usual care) (n=275), or usual care plus dietitian-delivered DASH-based dietary counselling in a single one-to-one session (intervention) (n=281). Primary outcomes were the changes in estimated 10-year CV risk.

Results: Outcome data were available for 504 (90.6%) and 485 (87.2%) patients at 6 and 12 months, respectively. There was no difference in the reduction of 10-year CV risk between the two groups at 6 months (-0.13%, 95% confidence interval [95%CI] -0.50% to 0.23%, p=0.477) and 12 months (-0.08%, 95%CI -0.33% to 0.18%, p=0.568). Multivariate regression analyses showed that male subjects, younger patients, current smokers, subjects with lower educational level, and those who dined out for main meals for ≥4 times in a typical week were significantly associated with no improvements in CV risk.

Conclusions: The findings may not support automatic referral of newly diagnosed grade 1 hypertensive patients for further one-to-one dietitian counselling. Patients with those risk factors identified should receive more clinical attention to reduce their CV risk. (250 words)

Clinical Trial Registration: ChiCTR-TRC-13003014 (http://www.chictr.org.cn/enindex.aspx)

Abbreviations: DASH, Dietary Approaches to Stop Hypertension; CV, cardiovascular; CI, confidence interval

Introduction

Uncontrolled high blood pressure (BP) remains a leading cause of cardiovascular disease (CVD), which plays a role in more than 31% of all global deaths [1]. The Dietary Approaches to Stop Hypertension (DASH) diet has been recommended in international guidelines for hypertension management [2-5]. Evidence mostly come from the original landmark trial [6] and subsequent feeding studies which demonstrated that short-term BP changes could lead to substantial reductions in BP [7-9]. Multi-factorial lifestyle components with multiple intervention sessions and frequent reminders were also adopted in DASH-series trials [10, 11], yet the long-term effectiveness of the DASH diet *per se*, if introduced into routine practice, is unclear.

Existing guidelines including the Seventh Report of the Joint National Committee, however, do not explicitly recommend how DASH should be delivered [2]. Trials that were designed to provide food to patients from research kitchens were relatively less applicable and feasible to clinical practice, wherein the one-off dietary counselling is most common in routine patient care. A previously described randomised controlled trial among grade 1 hypertensive patients in Hong Kong showed that one-off dietary counselling did not confer additional benefits on BP, body mass index, and lipid profiles [12]. Nevertheless, in light of the increasing atherosclerotic burden [13], it is uncertain whether DASH diet counselling could benefit patients in terms of reducing long-term cardio-vascular (CV) risks [14, 15]. To the best of our knowledge, no evidence exists as to whether patients newly diagnosed as having grade 1 hypertension should be referred to dietitian care for early DASH counselling, or just be offered brief advice on fundamental dietary principles from primary care physicians. A trial with CV risk as an outcome is important as it is widely recognised that patients with an estimated 10-year CV risk greater than 20% should be prescribed lipid-lowering agents, amongst other more intensive interventions.

This study tested the *a priori* hypothesis that one-off dietary counselling by dietitian based on the DASH recipe could reduce the estimated 10-year cardiovascular risk among hypertensive patients in real clinical setting. We also studied the factors independently associated with no improvements in cardiovascular risk among the same cohort of hypertensive patients recruited in primary care clinics.

Methods

Study design

A detailed description of the trial design has been reported [12]. This was a parallel-group, open-labelled, physician-blinded, randomised clinical trial with enrolment (January-March 2013) at two General Outpatient Clinics or at community health seminars through a primary care network in the New Territories East Cluster, Hong Kong. The study was approved by the Joint Chinese University of Hong Kong-New Territories East Cluster Clinical Research Ethics Committee, Hong Kong. The study protocol complied with the Declaration of Helsinki. The trial was prospectively registered (ChiCTR-TRC-13003014). Each trial participant provided written informed consent.

Patients

To be eligible, subjects had to be (1) Chinese patients aged 40-70 years; (2) newly diagnosed with grade 1 hypertension by trained clinical staffs according to a standard protocol [4]; and (3) currently receiving no antihypertensive drug therapies. The exclusion criteria were the presence of (1) medical conditions which required dietary control (e.g. diabetes and gout); (2) diseases with drug treatments that potentially interfered with the effectiveness of diet on the changes of blood lipid levels (e.g., obstructive sleep apnoea syndromes or dyslipidemia); (3) previous cardiovascular event. All participants verbally agreed to attend follow-up appointments at 6 and 12 months.

Randomisation and masking

Computer-generated numbers with a block size of 6 and an allocation ratio of 1:1 were used for group allocation. The research nurse opened the opaque envelope in which the randomised sequence was sealed, and then notified patients into either intervention or control group. The dietitian and study subjects were not masked to group allocation, but the attending physicians, research assistants, and clinical staff involved in the outcome data collection were blinded.

Procedures and risk factor measurement

Patient screening was performed to ascertain the subject eligibility. BP was determined by an automated sphygmomanometer device (ALPK2 DS-182) which was validated regularly. The BP was

measured in the right arm with the use of an appropriately sized cuff according to standardised protocol that was used in prior studies [16, 17]. BP measurements were obtained after the participants sat quietly for 5 minutes, at least one hour after the subject's last meal intake, and at least 30 minutes after cigarette smoking or consuming caffeinated beverages. The average of three BP measurements separated by at least 30 seconds were taken. Those with SBP of 140-159 mmHg and/or DBP of 90-99 mmHg were diagnosed as having grade 1 hypertension [4, 5]. A weight scale under periodic calibration was used to measure body weight in light clothing, and a wall-mounted stadiometer was used to measure body height without shoes. Usual care was provided to all participants (both groups). A DASH dietary counselling appointment was arranged immediately after usual care in the intervention arm only. Blood samples after an 8-hour fast were taken from all participants for measuring lipid profiles. The laboratory analysis was centrally undertaken at the Lek Yuen Health Centre, Hospital Authority, Hong Kong.

Usual care advice

Usual care was offered by the attending physician, following a standard educational pamphlet in which contents were tailored for hypertensive patients in all public primary care clinics in Hong Kong. The core components consisted of (1) the definition and aetiology of hypertension; (2) the diagnosis and possible complications of grade 1 hypertension; (3) annual assessment to ensure satisfactory BP control; and (4) general recommendations including smoking cessation, moderation of alcoholic consumption, weight reduction as appropriate, regular aerobic exercise, balanced diet with sodium reduction and reduced fat, as well as adequate sleep and rest. The format was standardised in a training workshop by the principal investigator (MCSW). The usual care lasted for 3-5 minutes, resembling the routine clinic practice.

DASH dietary counselling

Only subjects in the intervention arm received a further 25-minute one-off dietary counselling, offered by an experienced, registered dietitian (MKWM). The counselling was based on the DASH recipe [18] and were standardised in a pilot study to ensure that the counselling was feasible and intelligible to all participants. The contents included: (1) the nature and major components of the

DASH diet, (2) benefits of the diet, and (3) individualised meal plans that were tailored in Asia [19]. The individualised DASH diet goals were recommended with respect to high consumption of fruits (4-5 serves/day) and vegetables (4-5 serves/day), low-fat dairy products (2-3 serves/day), lean meats, poultry, and fish (≤6 serves/day), and nuts, seeds, and legumes (4-5 serves/week). The goals also included the achievement of limited intake of sweets, added sugars (≤5 serves/week), and fats and oils (2-3 serves/day) [18]. Reducing salt intake to less than 5 grams per day with no added salt use was also encouraged [19]. Participants were examined regarding their experiences with the counselling and the extent of understanding the DASH principles. The counselling process was documented for quality assurance.

Follow–up assessment

All participants attended follow-up clinic visits at 6 and 12 months with BP measurements and fasting blood samples taken. Subjects with abnormal BP or lipid levels (judged by the physicians) were referred to specialists. The dietary component intakes of the eight food groups (grains; vegetables; fruits; dairy; meat, poultry, fish, and eggs; nuts, seeds, and legumes; fats and oils; sweets) were assessed by a locally validated food frequency questionnaire [20, 21]. No significant between-arm differences were found, except that the intervention group reported marginally higher consumption of vegetables and diary at 12 months [12].

Outcomes

Primary outcomes were the changes in estimated 10-year risk of "hard" CV events comprising acute myocardial infarction, sudden death, and other coronary deaths [22]. A recalibrated and validated Chinese version of the Framingham equation derived from the Chinese Multi-provincial Cohort Study was used [22]. The estimated 10-year CV risk (P) is: $P=1-S(t)^{\exp(f[x,M])}$ $f(x,M)=Beta_1(x_1-M_1) + \ldots + Beta_p(x_p-M_p)$ where S(t) is the 10-year survival rate at the mean values of the risk factors; $Beta_1 \ldots Beta_p$ are the coefficients in the regression model; $x_1 \ldots x_p$ represent individual-level risk factors; and $M_1 \ldots M_p$ are the mean values of the risk factors in the cohort. Covariates included age, gender, and a series of modifiable CV risk factors including smoking status, BP, total cholesterol (TC), and high-density lipoprotein cholesterol (HDL-C). The algorithm followed the methods used in the Chinese

recalibration of the Framingham equation [22]. The effects of risk factors at differing ages and levels of the other risk factors are assumed constant [23]. The BP was categorised as optimal BP (having SBP <120 mmHg and DBP <80 mmHg with no antihypertensive medication taking), pre-hypertension (having SBP of 120-139 mmHg and/or DBP of 80-89 mmHg,), grade 1 hypertension, and grade 2-4 hypertension (having SBP ≥160 mmHg and/or DBP ≥100 mmHg). Cut-off points of 200 mg/dL (5.18 mmol/L) and 240 mg/dL (6.22 mmol/L) were applied to categorise the TC level into <160, 160-199, 200-239, 240-179, and ≥280 mg/dL. The HDL-C level was classified as <35 mg/dL (0.91 mmol/L), 35-44, 45-49, 50-59, and ≥60 mg/dL.

Statistical analysis

The primary outcomes were changes in the 10-year CV risk estimated on the basis of BP, TC, and HDL-C at 6 and 12 months, respectively. Secondary outcomes consisted of gender-stratified changes in CV risk factors between baseline and follow-ups. We aimed to detect an expected difference in DBP change of 2.0 mmHg at repeated follow-ups, which was considered clinically significant between the intervention and control arms. Previous literature reported a standard deviation of the DBP change of approximately 5.3 mmHg [6], and therefore we assumed a more conservative value of 7.0 mmHg in this study. The G*Power 3.1.0 gave a sample size of 252 per group that provided at least 85% power at the two-sided 5% significance level. A cumulative frequency analysis was conducted to illustrate the gender-stratified changes in BP at 12 months by groups. We fitted a linear-regression model in which analysis of covariance was performed to compare between-group differences (intervention minus usual care) in the changes of 10-year CV risk, with adjustment for the effects of other factors and baseline outcome measures. The last observation carried forward (LOCF) imputation method was used for managing missing data in sensitivity analysis. Factors associated with no improvements in the 10-year CV risks were initially evaluated by chi-square tests in univariate analysis, followed by a binary logistic regression analysis to test the association between all potentially independent variables and the outcome variable. A final regression model was then constructed using a backward stepwise algorithm that allowed for covariate re-entry with all covariates having p values of ≤0.10 retained in the model. Data analyses were performed in accordance with the CONSORT statement [24], using IBM SPSS Statistics 20.0 (Chicago, IL, USA).

Results

Participant characteristics

A total of 556 patients met the inclusion criteria and were randomised into either usual care (n=275, 49.5%) or DASH dietary counselling (n=281, 50.5%), respectively. At 6 and 12 months, 504 and 485 patients were available for analysis of the primary end-points **(CONSORT Figure 1)**. The first subject enrolled in January 2013, and the last subject completed the 12-month assessment in June 2014. The average age was 55.2 years and 49.1% were male. Baseline characteristics of the two groups were comparable across the background variables **(Table 1)**.

Changes in risk factors and estimated 10-year cardiovascular risk

None of the individual CV risk factors was significantly different between the two groups at baseline and 12 months **(Table 2)**. The reductions in BMI were observed in both groups with no significant between-group differences (-0.05, 95%CI -0.20 to 0.10, p=0.490). The crude cumulative percentage of subjects in the intervention group who experienced ≥2mmHg reduction in DBP or ≥3mmHg reduction in SBP were similar when compared to that in the control group. No significant between-group differences were detected for the magnitude of BP reductions **(Figure 2)**. Patients in both groups exhibited significant improvements in their 10-year CV risk over time simultaneously. The two groups, however, did not report any significant between-group difference in the changes of cardiovascular risk at 6 months (-0.13%, 95%CI -0.50% to 0.25%, p=0.477) and 12 months (-0.08%, 95% CI -0.33% to 0.18%, p=0.568) **(Table 3)**.

Factors associated with no improvements in 10-year cardiovascular risk

From binary logistic regression analysis with non-optimisation of cardiovascular risk as an outcome, it was found that male patients (adjusted odds ratio [aOR]=1.68, 95%CI 1.12 to 2.52, p=0.012), younger subjects (<55 years, aOR=1.49, 95%CI 1.00 to 2.23, p=0.049), current smokers (aOR=2.93, 95%CI 1.35 to 6.36, p=0.007), those with lower educational level (junior secondary or below, aOR=1.75, 95%CI 1.15 to 2.66, p=0.009) and subjects who dined out frequently for the main meal (aOR=1.85, 95%CI 1.03 to 3.32, p=0.038) were least likely to have their cardiovascular risk optimised **(Table 4)**.

Discussion

Statement of principle findings

This randomised clinical trial evaluated the effectiveness of dietitian counselling based on the DASH recipe among newly diagnosed grade 1 hypertensive patients in the real primary care setting. The estimated 10-year CV risk decreased significantly in both groups from baseline to 12 months, yet the DASH counselling produced no additional benefits. Male subjects, younger patients, current smokers, subjects with lower educational level, and those who dined out frequently were less likely to be benefited from the dietary counselling to the optimisation of CV risk. These findings may not support the value of automatic referral of grade 1 hypertensive patients to one-off dietitian care when newly diagnosed. Patients with risk factors identified in this study warrant more clinical attention as they might be more resistant to CV risk improvement over time.

Relationship with other studies

The effectiveness of the DASH diet was largely established on the basis of previous controlled feeding trials, which indicated that individuals given prepared or prescribed DASH diet had lower BP, compared with controls [6-9, 15]. The DASH diet, as a result of these trials conducted in the research kitchen context, was recommended in most hypertension guidelines [2-5, 25] - and also an example of healthful eating pattern [26]. The US Nurses Health longitudinal study showed that the long-term adherence to DASH-style diet could benefit healthy female nurses with regard to reduced CV risk [27]. Nevertheless, both studies performed in research kitchen and among free-living health-conscious adults carried the underlying nature of optimum adherence to the DASH diet. The compliance may also be substantially optimised by intensive reminders, weekly peer-group sessions, daily food consumption diaries [28], or multiple intervention sessions with calorie and nutrient intake monitoring [10, 11]. Our study, in contrast, was performed in the real clinical setting wherein the dietary counselling practices are often delivered to grade 1 hypertensive patients on a one-off basis without follow-up prompts [29-31].

Previous translational efforts have been made to estimate the overall effect of DASH diet on CV risk estimates on the basis of risk factors, given the cost and logistical consideration of long-term trial with

"hard" CV events as the actual clinical endpoint [32]. The Framingham-based risk equation [22, 33] was a widely-used risk prediction algorithm to estimate 10-year CV risk. An earlier meta-regression analysis of randomised trials showed that being overweight made the largest contribution to hypertension [34]. The short-term effect of consuming reduced fats and oils in the DASH diet on cholesterol could be therefore more apparent for overweight people who lose weight [35]. In our trial, the study participants in both groups demonstrated weight reductions with similar magnitude on follow-ups. We did not specifically collect information on the dietary intakes of fatty acid in the two groups, and therefore we could not rule out the possibility that subjects in the intervention group may also have reduced intake of unsaturated fat when limiting the overall consumption of dietary fats and oils simultaneously. Albeit the intake of unsaturated fat may affect HDL-C level (one of the components of the Framingham risk equation), it is not likely that the intake changes can explain the relative absence of intervention effects as no significant between-group differences in the changes of lipid levels were detected in the present study. The original DASH study had the potential to decrease estimated 10-year CV risk by 18% [36]. In the PREMIER study, subjects who received the DASH diet plus combined multi-component lifestyle behavioural modifications had similar decrease in 10-year CV risk when compared to the advice-only control at 6 months, but reported significantly reduced risk by 12% at 18 months [10, 37]. Another US study has shown a decreased 10-year CV risk by 12.1% from an 8-week DASH diet feeding [38]. We used a Chinese version of the Framingham equation in which the relationship between changes in estimated 10-year CV risk with actual subsequent CV event was recalibrated and validated [22]. The reduction of predicted 10-year CV risk by 19.3% (dropped from 3.37% to 2.72% at 12 months) observed in the intervention group was comparable to that in previous studies, implying the validity of the trial fidelity. Moreover, a CV risk reduction by 17.1% (dropped from 2.98% to 2.47% at 12 months) in the control arm with no between-group differences therefore suggesting favourable effects in both groups.

Meaning of the study

Given that the DASH diet has been adopted in hypertension guidelines and reference frameworks for hypertension care, we would not regard our work as a simple replication study of previous trials. By contrast, our trial provides data for the intervention as adapted for implementation in real-world

clinical setting wherein both the DASH diet and the dietitian-delivered counselling in a single one-to-one session were tested as a combined intervention. We showed similarity in responses in the reduction of 10-year CV risk between intervention and control groups. One may criticise the inadequate "dose" of the DASH diet from a one-off counselling session; albeit it is relatively rare for real-world dietary counselling to be offered more frequently than once a year particularly among those with newly diagnosed mildly-elevated BP [29-31]. The real-life dietary adherence may also be influenced by contextual factors such as the costs of foods and the taste of low-fat foods, as evidence revealing that the concordance with the DASH diet tended to be lower in free-living population [39]. Moreover, both the UK and US studies have argued that greater accordance with the DASH food group targets could be associated with higher dietary costs indeed [40, 41]. This may suggest a reconsideration of the DASH diet given the cultural acceptability and structural barriers to modifying eating habits, despite that we were unable to account for the cost-effectiveness in the present trial. The US National Health and Nutrition Examination Survey (NHANES) data illustrated that only around 1 in 5 individuals practically followed an eating plan modelled on the DASH diet in daily life [42]. It has been argued that the limited time spent on providing adequate instructions due to the reimbursement structure in the US healthcare context [42] may be at play. Our study has prolonged the dietitian-patient consultation time to almost 30 minutes with detailed educational materials, yet the similar magnitude in the CV risk reductions obtained in both groups implied that the prior assumption related to dietary counselling itself may be misstated.

Our study showed that factors associated with lower odds of CV risk improvements included younger age and lower education level, which were echoed in a number of other studies that reported the decreased likelihood of changing dietary patterns among these subjects [42]. We reported differences in responses in the CV risk reductions between males and females. This was undertaken *post hoc* due to observed differences, and the exploratory results should be interpreted cautiously. The initial CV risk was relatively lower for males, which might reduce the chance of achieving significant changes following the intervention, albeit the baseline differences were controlled for in the analysis. Further study specifically designed to allow separate gender analyses may elucidate the gender-specific responses. The study recruitment was conducted in Hong Kong, where dinning out is an integral part

of its culture. Subjects who often go out for the main meal of the day were less likely to optimise 10-year CV risk. This supports the criticism on the widespread dining-out trend with fast-food culture which appears to embrace rich calorie and poor nutrient [13, 42].

The study findings are the most directly applicable to routine practice in the Chinese population, with wider relevance to primary prevention in health-care system in other middle- and low- income countries. The standard education from physician's usual care advice alone in this study has shown a persistent BP reduction by an amount similar to that achieved with additive DASH-based dietary counselling. This implied that usual physician care alone might be adequate to maintain a significant improvement in CV risk over time, and if translated into clinical practice, one could expect substantial cost-saving. The possibility of reducing or avoiding further dietitian referral could lead to substantial clinical benefits in terms of streamlined counselling process and public health impact with regard to cutting unnecessary cost to individuals and the healthcare system.

Strengths and weaknesses of the study

This randomised controlled trial was sufficiently powered and included subjects who were treatment-naive to both antihypertensive medications and other community-based programs. All individuals were newly-diagnosed, and patients with other medical conditions requiring dietary modification were excluded to eliminate possible confounder effects. The similarity of baseline characteristics between the two groups and the strict adherence with study protocols further improved the internal validity and robustness of the findings. The vast majority of patients received no drug treatments during the entire study period. The proportions of individuals who developed comorbidities or received further drug treatments for safety reasons were relatively small, and were similar between the two arms. In the sensitivity analysis wherein the LOCF imputation methods were applied for missing data (less than 10%) and patients with drug therapies were excluded, similar findings were yielded. Nevertheless, weakness of this study should receive attention. Firstly, we used 10-year CV risk estimates instead of actual CV events as the primary outcome. A universal critique might be the accuracy and validity with respect to how closely the predicted outcomes agree with the actual outcomes. However, the Chinese version of the risk equation has been validated in the ethnic Chinese who comprised the entire study

population in our trial. The use of risk estimation instead of the incidence of actual CV events after 10 years allows greater feasibility of trial implementation with higher retention rate. Secondly, the 10-year CV risk presented at baseline was relatively low due to the nature of mild hypertension, and the Hawthorne effect [43] in the clinic-based data collection may exist, which could be partially responsible for the lack of effect in the intervention group. Nevertheless, the study participants in the physician's usual care group still reported a significant CV risk reduction similar to those in the intervention group. This could be broadly applied to the general population with wider relevance to primary prevention.

Conclusions

The automatic referral of newly diagnosed grade 1 hypertensive patients for further one-to-one dietitian counselling in a single session may not be supported on the basis of the trial evidence found for its effectiveness in the routine clinical setting. More clinical attention are required on male subjects, younger patients, current smokers, subjects with lower educational level, and those frequent dine-outers, as they were less likely to be responsive to long-term CV risk improvements. It is possible that adding more intensive or multiple intervention sessions might shift the evidentiary balance in favour of the intervention; however, usual physician care alone might be adequate to maintain a significant improvement in CV risk over time. One may therefore expect substantial cost-saving in middle- and low-income countries wherein primary care physicians are being strengthened as the locus of responsibility for the long-term care.

Source(s) of Funding: This work was supported by grants from the Health and Medical Research Fund, Food and Health Bureau, Hong Kong Government (09100701) led by M.C.S. Wong at The Chinese University of Hong Kong. H.H.X. Wang was supported by New Faculty Start-Up Research Fund (51000-31121405 and 51000-18821202) at Sun Yat-Sen University. The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Competing interests: The author(s) declare that they have no competing interests.

Authors' contributions: MCSW and HHXW conceived of the study design and provided overall guidance. BCYF, STSL, ML, FTHF, and MSY contributed to the administrative, technical, and material support. Data analysis was mainly done by HHXW and MWMK. All authors contributed to literature search and interpretation of the data. MCSW and HHXW wrote the first draft. MWMK and STSL contributed to the subsequent revisions of the manuscript. All authors contributed to the feedback on study results and critical revisions of the final report for important intellectual content. All authors, external and internal, had full access to all of the data (including statistical reports and tables) in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis

Acknowledgments: We wish to thank our research collaborators at The Chinese University of Hong Kong, especially Jean Woo for her valuable inputs in the outcome measures, and William Goggins for his valuable advice in the statistical analysis. This work was supported by grants from the Health and Medical Research Fund, Food and Health Bureau, Hong Kong Government (09100701) led by M.C.S. Wong at The Chinese University of Hong Kong. H.H.X. Wang was supported by New Faculty Start-Up Research Fund (51000-31121405 and 51000-18821202) at Sun Yat-Sen University.

References

[1] Mendis S. Global Status Report on Noncommunicable Diseases 2014: World Health Organization; 2014.

[2] Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL, et al. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure - The JNC 7 Report. *JAMA* 2003;289:2560-72.

[3] Williams B, Poulter NR, Brown MJ, Davis M, McInnes GT, Potter JF, et al. British Hypertension Society guidelines for hypertension management 2004 (BHS-IV): summary. *BMJ* 2004;328:634-40.

[4] Mancia G, Fagard R, Narkiewicz K, Redon J, Zanchetti A, Bohm M, et al. 2013 ESH/ESC guidelines for the management of arterial hypertension: the Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *Eur Heart J* 2013;34:2159-219.

[5] Mancia G, Fagard R, Narkiewicz K, Redon J, Zanchetti A, Bohm M, et al. 2013 ESH/ESC Guidelines for the management of arterial hypertension: the Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *J Hypertens* 2013;31:1281-357.

[6] Appel LJ, Moore TJ, Obarzanek E, Vollmer WM, Svetkey LP, Sacks FM, et al. A clinical trial of the effects of dietary patterns on blood pressure. DASH Collaborative Research Group. *N Engl J Med* 1997;336:1117-24.

[7] Sacks FM, Svetkey LP, Vollmer WM, Appel LJ, Bray GA, Harsha D, et al. Effects on blood pressure of reduced dietary sodium and the dietary approaches to stop hypertension (DASH) diet. *N Engl J Med* 2001;344:3-10.

[8] Miller ER, Erlinger TP, Young DR, Jehn M, Charleston J, Rhodes D, et al. Results of the Diet, Exercise, and Weight loss Intervention Trial (DEW-IT). *Hypertension* 2002;40:612-8.

[9] Appel LJ, Sacks FM, Carey VJ, Obarzanek E, Swain JF, Miller ER, et al. Effects of protein, monounsaturated fat, and carbohydrate intake on blood pressure and serum lipids - Results of the OmniHeart randomized trial. *JAMA* 2005;294:2455-64.

[10] Appel LJ, Champagne CM, Harsha DW, Cooper LS, Obarzanek E, Elmer PJ, et al. Effects of comprehensive lifestyle modification on blood pressure control: main results of the PREMIER clinical trial. *JAMA* 2003;289:2083-93.

[11] Lien LF, Brown AJ, Ard JD, Loria C, Erlinger TP, Feldstein AC, et al. Effects of PREMIER lifestyle modifications on participants with and without the metabolic syndrome. *Hypertension* 2007;50:609-16.
[12] Wong MCS, Wang HHX, Kwan MWM, Fong BCY, Chan WM, Zhang DX, et al. Dietary counselling has no effect on cardiovascular risk factors among Chinese Grade 1 hypertensive patients: a randomized controlled trial. *Eur Heart J* 2015;36:2598-607.
[13] Wong MCS, Zhang DX, Wang HHX. Rapid emergence of atherosclerosis in Asia: a systematic review of coronary atherosclerotic heart disease epidemiology and implications for prevention and control strategies. *Curr Opin Lipidol* 2015;26:257-69.
[14] Kwan MWM, Wong MCS, Wang HHX, Liu KQL, Lee CLS, Yan BP, et al. Compliance with the Dietary Approaches to Stop Hypertension (DASH) diet: a systematic review. *Plos One* 2013;8:e78412.
[15] Saneei P, Salehi-Abargouei A, Esmaillzadeh A, Azadbakht L. Influence of Dietary Approaches to Stop Hypertension (DASH) diet on blood pressure: a systematic review and meta-analysis on randomized controlled trials. *Nutr Metab Cardiovasc Dis* 2014;24:1253-61.
[16] Wang HHX, Wong MCS, Mok RY, Kwan MWM, Chan WM, Fan CKM, et al. Factors associated with grade 1 hypertension: implications for hypertension care based on the Dietary Approaches to Stop Hypertension (DASH) in primary care settings. *BMC Fam Pract* 2015;16:26.
[17] Wong MCS, Liu KQL, Wang HHX, Lee CLS, Kwan MWM, Lee KW, et al. Effectiveness of a pharmacist-led drug counseling on enhancing antihypertensive adherence and blood pressure control: a randomized controlled trial. *J Clin Pharmacol* 2013;53:753-61.
[18] Your guide to lowering your blood pressure with DASH (06-5834): National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, MD 20892; 2006.
[19] Module 5: Dietary Intervention. Hong Kong Reference Framework for Hypertension Care for Adults in Primary Care Settings: Department of Health, The Government of Hong Kong Special Administrative Region; 2013.
[20] Sea MMM, Woo J, Tong PCY, Chow CC, Chan JCN. Associations between food variety and body fatness in Hong Kong Chinese adults. *J Am Coll Nutr* 2004;23:404-13.
[21] Yu R, Woo J, Chan R, Sham A, Ho S, Tso A, et al. Relationship between dietary intake and the development of type 2 diabetes in a Chinese population: the Hong Kong Dietary Survey. *Public Health Nutr* 2011;14:1133-41.

[22] Liu J, Hong Y, D'Agostino RB, Sr., Wu Z, Wang W, Sun J, et al. Predictive value for the Chinese population of the Framingham CHD risk assessment tool compared with the Chinese Multi-Provincial Cohort Study. *JAMA* 2004;291:2591-9.
[23] Cooney MT, Dudina A, D'Agostino R, Graham IM. Cardiovascular risk-estimation systems in primary prevention: do they differ? Do they make a difference? Can we see the future? *Circulation* 2010;122:300-10.
[24] Moher D, Hopewell S, Schulz KF, Montori V, Gotzsche PC, Devereaux PJ, et al. CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trials. *BMJ* 2010;340:c869.
[25] Clinical Practice Guidelines on Management of Hypertension (4th Edition): The Malaysian Society of Hypertension (MSH); 2014.
[26] Committee DGA. Report of the Dietary Guidelines Advisory Committee on the Dietary Guidelines for Americans, 2010, to the Secretary of Agriculture and the Secretary of Health and Human Services. *Agricultural Research Service* 2010.
[27] Fung TT, Chiuve SE, McCullough ML, Rexrode KM, Logroscino G, Hu FB. Adherence to a DASH-style diet and risk of coronary heart disease and stroke in women. *Arch Intern Med* 2008;168:713-20.
[28] Lara J, Evans EH, O'Brien N, Moynihan PJ, Meyer TD, Adamson AJ, et al. Association of behaviour change techniques with effectiveness of dietary interventions among adults of retirement age: a systematic review and meta-analysis of randomised controlled trials. *BMC Med* 2014;12:177.
[29] Krause T, Lovibond K, Caulfield M, McCormack T, Williams B, Group GD. Management of hypertension: summary of NICE guidance. *BMJ* 2011;343:d4891.
[30] Duggan K, Anderson C, Arnolda L, Boyden A, Cowley D, Dart A, et al. Guide to the Management of Hypertension 2008 - Assessing and managing raised blood pressure in adults: National Heart Foundation of Australia; 2008.
[31] Luehr D, Woolley T, Burke R, Dohmen F, Hayes R, Johnson M, et al. Hypertension diagnosis and treatment. NGC:009522. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2012.
[32] Lloyd-Jones DM. Cardiovascular risk prediction: basic concepts, current status, and future directions. *Circulation* 2010;121:1768-77.

[33] D'Agostino RB, Sr., Grundy S, Sullivan LM, Wilson P, Group CHDRP. Validation of the Framingham coronary heart disease prediction scores: results of a multiple ethnic groups investigation. *JAMA* 2001;286:180-7.

[34] Geleijnse JM, Kok FJ, Grobbee DE. Impact of dietary and lifestyle factors on the prevalence of hypertension in Western populations. *Eur J Public Health* 2004;14:235-9.

[35] Azadbakht L, Mirmiran P, Esmaillzadeh A, Azizi T, Azizi F. Beneficial effects of a Dietary Approaches to Stop Hypertension eating plan on features of the metabolic syndrome. *Diabetes Care* 2005;28:2823-31.

[36] Chen ST, Maruthur NM, Appel LJ. The effect of dietary patterns on estimated coronary heart disease risk: results from the Dietary Approaches to Stop Hypertension (DASH) trial. *Circ Cardiovasc Qual Outcomes* 2010;3:484-9.

[37] Maruthur NM, Wang NY, Appel LJ. Lifestyle interventions reduce coronary heart disease risk: results from the PREMIER Trial. *Circulation* 2009;119:2026-31.

[38] Obarzanek E, Sacks FM, Vollmer WM, Bray GA, Miller ER, 3rd, Lin PH, et al. Effects on blood lipids of a blood pressure-lowering diet: the Dietary Approaches to Stop Hypertension (DASH) Trial. *Am J Clin Nutr* 2001;74:80-9.

[39] Jiang J, Liu M, Troy LM, Bangalore S, Hayes RB, Parekh N. Concordance with DASH diet and blood pressure change: results from the Framingham Offspring Study (1991-2008). *J Hypertens* 2015;33:2223-30.

[40] Monsivais P, Rehm CD, Drewnowski A. The DASH diet and diet costs among ethnic and racial groups in the United States. *JAMA Intern Med* 2013;173:1922-4.

[41] Monsivais P, Scarborough P, Lloyd T, Mizdrak A, Luben R, Mulligan AA, et al. Greater accordance with the Dietary Approaches to Stop Hypertension dietary pattern is associated with lower diet-related greenhouse gas production but higher dietary costs in the United Kingdom. *Am J Clin Nutr* 2015;102:138-45.

[42] Mitka M. DASH dietary plan could benefit many, but few hypertensive patients follow it. *JAMA* 2007;298:164-5.

[43] McCambridge J, Witton J, Elbourne DR. Systematic review of the Hawthorne effect: new concepts are needed to study research participation effects. *J Clin Epidemiol* 2014;67:267-77.

Figure Legends

CONSORT Figure 1: Profile of the Randomised Clinical Trial

Figure 2: Cumulative frequency analysis of the changes in blood pressure at 12 month

CONSORT Figure 1: Profile of the Randomised Clinical Trial

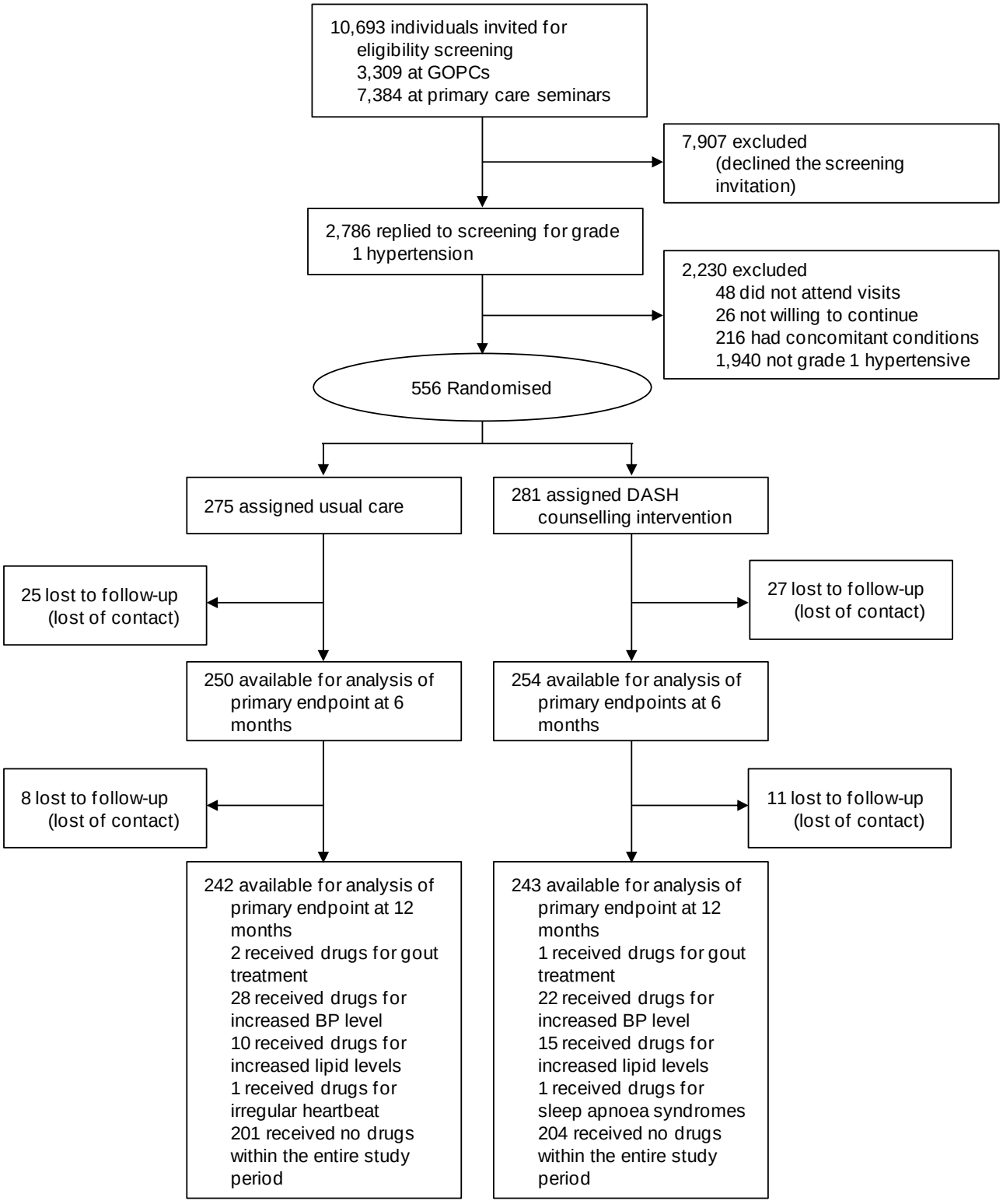
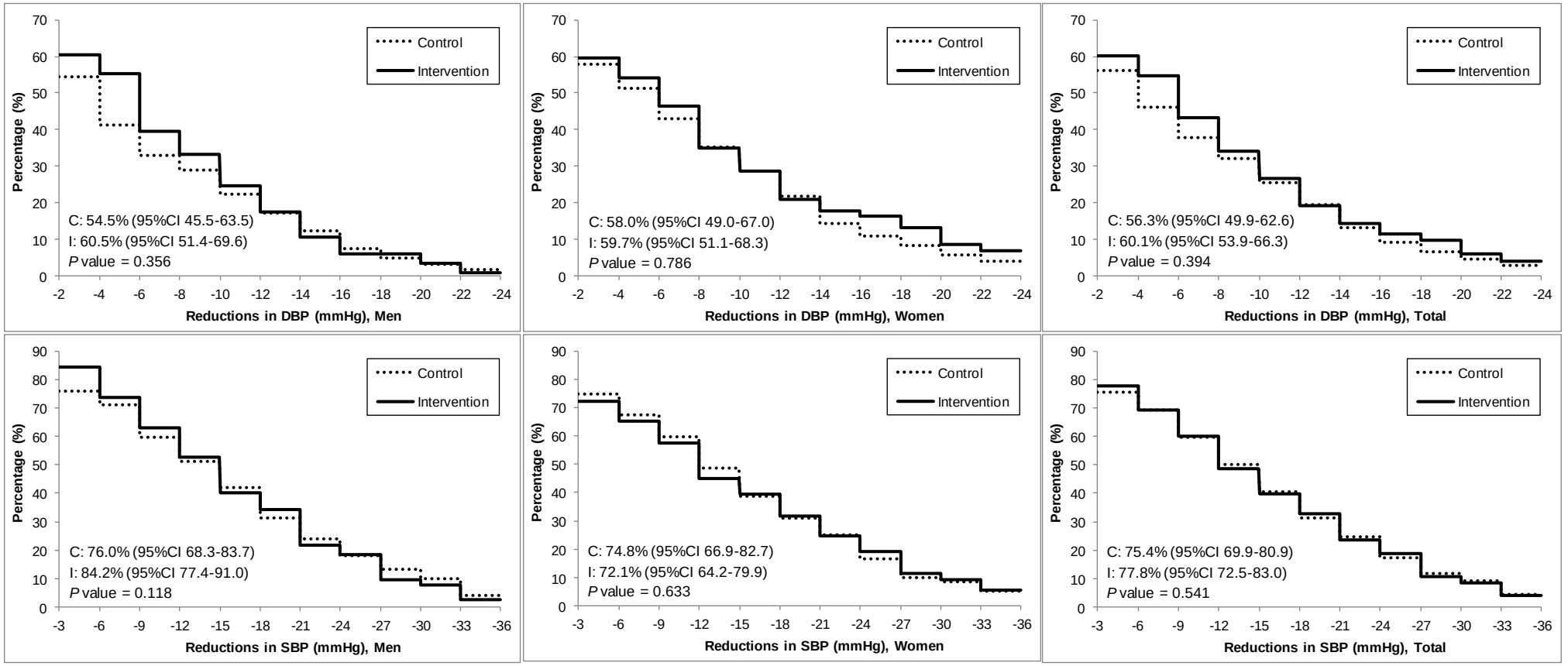


Figure 2: Cumulative frequency analysis of the changes in blood pressure at 12 months



DBP, diastolic blood pressure; SBP, systolic blood pressure.

Table Legends:

Table 1: Background characteristics of the trial participants

Table 2: Change of CV risk factors in the Framingham equation in the usual care group and DASH counselling group from baseline to 12 months

Table 3: Estimated absolute 10-year CV events (%) in the usual care group and DASH counselling group

Table 4: Factors associated with no improvements in 10-year CV risks

Table 1: Background characteristics of the trial participants

Characteristic	Usual care group (n=275)	DASH counselling group (n=281)	*P* value	All participants (N=556)
Sex (M/F)	142/133	131/150	0.237*	273/ 283
Males				
Age, years	54.7 (5.0)	55.4 (5.0)	0.980	55.0 (5.0)
BMI, kg/m^2	24.28 (2.85)	24.53 (2.58)	0.389	24.40 (2.72)
SBP, mmHg	143.7 (7.6)	144.3 (7.4)	0.503	144.0 (7.5)
DBP, mmHg	90.9 (5.6)	91.7 (5.5)	0.220	91.3 (5.6)
TC, mmol/L	5.39 (0.88)	5.45 (0.78)	0.556	5.41 (0.83)
HDL-C, mmol/L	1.43 (0.41)	1.41 (0.35)	0.619	1.42 (0.38)
LDL-C, mmol/L	3.27 (0.78)	3.41 (0.77)	0.157	3.33 (0.78)
TG, mmol/L	1.48 (0.78)	1.38 (0.81)	0.275	1.43 (0.80)
Senior education or above	101 (71.6)	90 (69.8)	0.737*	191 (70.7)
Family history of hypertension	97 (68.8)	84 (64.6)	0.466*	181 (66.8)
Current smokers	16 (11.3)	15 (11.6)	0.942*	31 (11.5)
Comorbidities	0.14 (0.42)	0.16 (0.40)	0.794	0.15 (0.41)
Females				
Age, years	55.2 (5.3)	55.3 (6.0)	0.222	55.3 (5.7)
BMI, kg/m^2	24.15 (3.31)	23.82 (3.00)	0.438	23.98 (3.15)
SBP, mmHg	146.2 (6.9)	146.0 (8.1)	0.743	146.1 (7.5)
DBP, mmHg	89.0 (7.2)	89.4 (8.1)	0.667	89.2 (7.7)
TC, mmol/L	5.45 (0.76)	5.62 (0.83)	0.078	5.54 (0.80)
HDL-C, mmol/L	1.67 (0.42)	1.66 (0.45)	0.811	1.67 (0.44)
LDL-C, mmol/L	3.24 (0.74)	3.37 (0.84)	0.159	3.31 (0.79)
TG, mmol/L	1.18 (0.56)	1.30 (0.61)	0.096	1.25 (0.59)
Senior education or above	62 (47.0)	70 (47.6)	0.914*	132 (47.3)
Family history of hypertension	94 (71.2)	102 (69.4)	0.739*	196 (70.3)
Current smokers	2 (1.5)	1 (0.7)	0.500*	3 (1.1)
Comorbidities	0.28 (0.56)	0.22 (0.52)	0.404	0.25 (0.54)

Values are presented as mean (SD) for continuous variables and number (%) for categorical variables. SD, standard deviation; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; HDL-C, high-density lipoprotein-cholesterol; LDL-C, low-density lipoprotein-cholesterol; TG, triglyceride.

* Use of chi-square tests

Table 2: Change of CV risk factors in the Framingham equation in the usual care group and DASH counselling group from baseline to 12 months

Risk Factors	Baseline			12 months		
	Usual care	Intervention	*P*	Usual care	Intervention	*P*
Males						
Blood Pressure			--			0.880
Optimal	0 (0.0)	0 (0.0)		7 (5.7)	9 (7.9)	
Pre-hypertension	0 (0.0)	0 (0.0)		41 (33.6)	38 (33.3)	
Grade 1 hypertension	142 (100.0)	131 (100.0)		65 (53.3)	57 (50.0)	
Grade 2-4 hypertension	0 (0.0)	0 (0.0)		9 (7.4)	10 (8.8)	
TC, mg/dL			0.858			0.712
<160	12 (9.0)	7 (5.9)		8 (6.6)	5 (4.5)	
160-199	43 (32.3)	39 (32.8)		50 (41.0)	49 (44.5)	
200-239	57 (42.9)	53 (44.5)		48 (39.3)	46 (41.8)	
240-279	20 (15.0)	18 (15.1)		15 (12.3)	10 (9.1)	
≥280	1 (0.8)	2 (1.7)		1 (0.8)	0 (0.0)	
HDL-C, mg/dL			0.745			0.503
<35	9 (6.8)	8 (6.7)		8 (6.6)	5 (4.5)	
35-44	27 (20.3)	20 (16.8)		29 (23.8)	17 (15.5)	
45-49	14 (10.5)	13 (10.9)		12 (9.8)	12 (10.9)	
50-59	39 (29.3)	44 (37.0)		34 (27.9)	37 (33.6)	
≥60	44 (33.1)	34 (28.6)		39 (32.0)	39 (35.5)	
Females						
Blood Pressure			--			0.748
Optimal	0 (0.0)	0 (0.0)		9 (7.5)	8 (6.2)	
Pre-hypertension	0 (0.0)	0 (0.0)		47 (39.2)	44 (34.1)	
Grade 1 hypertension	133 (100.0)	150 (100.0)		47 (39.2)	59 (45.7)	
Grade 2-4 hypertension	0 (0.0)	0 (0.0)		17 (14.2)	18 (14.0)	
TC, mg/dL			0.155			0.760
<160	7 (5.5)	4 (2.8)		7 (5.9)	5 (3.8)	
160-199	41 (32.0)	40 (28.0)		40 (33.6)	39 (30.0)	
200-239	56 (43.8)	61 (42.7)		51 (42.9)	58 (44.6)	
240-279	24 (18.8)	33 (23.1)		20 (16.8)	25 (19.2)	
≥280	0 (0.0)	5 (3.5)		1 (0.8)	3 (2.3)	
HDL-C, mg/dL			0.905			0.589
<35	2 (1.6)	1 (0.7)		3 (2.5)	2 (1.5)	
35-44	10 (7.8)	11 (7.7)		9 (7.6)	11 (8.5)	
45-49	10 (7.8)	9 (6.3)		2 (1.7)	7 (5.4)	
50-59	32 (25.0)	41 (28.7)		29 (24.4)	30 (23.1)	
≥60	74 (57.8)	81 (56.6)		76 (63.9)	80 (61.5)	

Values are presented as number (%). TC, total cholesterol; HDL-C, high-density lipoprotein-cholesterol.

Table 3: Estimated absolute 10-year CV events (%) in the usual care group and DASH counselling group

Ten-year risk (%)	Mean (SD)			Within-group differences (95%CI)*				Between-group differences (95%CI)†			
	Baseline	6 months	12 months	6 months	*P*	12 months	*P*	6 months	*P*	12 months	*P*
Males											
Usual care	2.12 (1.43)	1.90 (1.39)	1.90 (1.22)	-0.22 (-0.35 to -0.09)	0.001	-0.22 (-0.35 to -0.10)	0.001	--		--	
Intervention	2.31 (1.42)	1.98 (1.27)	1.94 (1.20)	-0.34 (-0.50 to -0.17)	<0.001	-0.38 (-0.53 to -0.22)	<0.001	--		--	
Intervention *vs* usual care	--			--				-0.12 (-0.33 to 0.08)	0.244	-0.16 (-0.36 to 0.04)	0.111
Females											
Usual care	3.88 (4.85)	3.58 (4.96)	3.07 (4.14)	-0.30 (-0.70 to 0.10)	0.135	-0.82 (-1.16 to -0.48)	<0.001	--		--	
Intervention	4.28 (5.07)	3.81 (5.83)	3.39 (4.04)	-0.47 (-1.01 to 0.08)	0.094	-0.89 (-1.25 to -0.52)	<0.001	--		--	
Intervention *vs* usual care	--			--				-0.13 (-0.82 to 0.56)	0.717	-0.03 (-0.49 to 0.42)	0.889
Total											
Usual care	2.98 (3.64)	2.72 (3.70)	2.47 (3.07)	-0.26 (-0.47 to -0.06)	0.013	-0.51 (-0.69 to -0.33)	<0.001	--		--	
Intervention	3.37 (3.96)	2.96 (4.45)	2.72 (3.15)	-0.41 (-0.71 to -0.10)	0.009	-0.65 (-0.86 to -0.44)	<0.001	--		--	
Intervention *vs* usual care	--			--				-0.13 (-0.50 to 0.23)	0.477	-0.08 (-0.33 to 0.18)	0.568

CHD, coronary heart disease; SD, standard deviation; CI, confidence interval.

*Differences were calculated from 6-month follow-up between baseline, and 12-month follow-up between baseline, respectively.

†Adjusted for gender, age, BMI, route into study (general outpatient clinics, or responding to the invitations from community health seminars), level of education, monthly household income, family history of hypertension, number of comorbidities, and baseline blood pressure measures.

Table 4: Factors associated with no improvements in 10-year CV risks

	Model 1		Model 2*		Model 3†	
Variable	**cOR (95%CI)**	***P***	**aOR (95%CI)**	***P***	**aOR (95%CI)**	***P***
Gender, male	1.24 (0.87 - 1.77)	0.227	1.60 (1.03 - 2.49)	0.035	1.68 (1.12 - 2.52)	0.012
Age, <55 years	1.35 (0.94 - 1.93)	0.107	1.50 (0.99 - 2.28)	0.057	1.49 (1.00 - 2.23)	0.049
Current smokers	1.77 (0.90 - 3.48)	0.099	2.86 (1.26 - 6.45)	0.012	2.93 (1.35 - 6.36)	0.007
Education, ≤ junior secondary	1.14 (0.80 - 1.63)	0.474	1.85 (1.19 - 2.90)	0.007	1.75 (1.15 - 2.66)	0.009
Dining out	1.60 (0.92 - 2.78)	0.095	1.89 (1.05 - 3.41)	0.034	1.85 (1.03 - 3.32)	0.038
Current drinker	1.32 (0.76 - 2.27)	0.324	1.09 (0.56 - 2.11)	0.800	--	
Family history of hypertension						
No history	1.00 (Ref)		1.00 (Ref)		--	
Presence	0.90 (0.61 - 1.33)	0.591	0.88 (0.58 - 1.33)	0.539		
Treatment						
Usual care	1.00 (Ref)		1.00 (Ref)		--	
DASH counselling	1.01 (0.71 - 1.43)	0.970	0.99 (0.68 - 1.44)	0.952		
Household income /month						
<US$1,290	1.00 (Ref)		1.00 (Ref)		--	
$1,290 - $2,579	1.18 (0.63 - 2.19)	0.607	0.95 (0.48 - 1.89)	0.882		
$2,580 - $3,869	1.29 (0.68 - 2.46)	0.439	1.03 (0.50 - 2.10)	0.941		
$3,870 - $5,159	1.71 (0.89 - 3.28)	0.106	1.45 (0.70 - 3.02)	0.318		
≥$5,160	1.46 (0.79 - 2.71)	0.229	1.18 (0.56 - 2.46)	0.666		
Comorbidities						
No comorbidities	1.00 (Ref)		1.00 (Ref)		--	
With comorbidities	1.30 (0.41 - 4.10)	0.653	1.40 (0.38 - 5.18)	0.617		

cOR, crude odds ratio; aOR, adjusted odds ratio; CI, confidence interval; Ref, reference; DASH, Dietary Approaches to Stop Hypertension. Current smokers referred to those who were currently smoking tobacco on a consistent basis as regular lifestyle behaviour. Dining out refers to going out for the main meal of the day more than 4 times in a typical week.

*Model 2 adjusted for other independent variables listed.

†Model 3 (final model) was constructed using a backward stepwise algorithm that allowed for covariate re-entry with all covariates having *p* values of ≤0.10 retained in the model.

CONSORT Checklist

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Trial Protocol

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