

## **Dietary patterns and hearing loss in older men enrolled in the Caerphilly Study.**

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### **List of abbreviations**

CVD= Cardiovascular disease

dB= decibel

dB<sub>A</sub>= unaided pure-tone binaural threshold

DP= Dietary pattern

FFQ= Food frequency questionnaire

OR= Odds ratio

PCA= Principal component analysis

PTA= Pure-tone average

WI= Weighed food intake

## ABSTRACT

The association between dietary patterns (DPs) and prevalence of hearing loss in men enrolled in the Caerphilly Prospective Study was investigated. The study recruited 2,512 men aged 45-59 years during 1979-1983. At baseline, dietary data were collected using a semi-quantitative food frequency questionnaire (FFQ), and 7-day weighed food intake (WI) in a 30% sub-sample. Pure-tone unaided audiometric threshold was assessed at 0.5, 1, 2 and 4 kHz, five years later. Principal component analysis (PCA) identified three DPs and multiple logistic and ordinal logistic regression models were fitted to examine associations with hearing loss (defined as pure-tone average (PTA) of frequencies 0.5, 1, 2 and 4 kHz greater than 25 decibels (dB)). Traditional, Healthy and High sugar/Low alcohol DPs were derived from PCA of both FFQ and WI data. With the FFQ data, fully adjusted models demonstrated significant inverse associations between the Healthy DP and both hearing loss as a dichotomous variable (OR=0.83; 95% CI=0.77, 0.90; P<0.001) and as an ordinal variable (OR=0.87; 95% CI=0.81, 0.94; P<0.001). With the WI data, fully adjusted models showed a significant and inverse association between the Healthy DP and hearing loss (OR=0.85; 95% CI=0.73, 0.99; P<0.03), and a significant association between the Traditional DP (per fifth increase) and both hearing loss as a dichotomous variable (OR=1.18; 95% CI=1.02, 1.35; P=0.02), and as an ordinal variable (OR= 1.17; 95% CI=1.03, 1.33); P=0.02). A Healthy DP was significantly and inversely associated with hearing loss in older men. The role of diet in age-related hearing loss warrants further investigation.

## INTRODUCTION

Hearing loss is highly prevalent in older people and can reduce quality of life substantially<sup>(1,2)</sup>, with detrimental effects on emotional health<sup>(3–5)</sup> and on cognitive function<sup>(6–8)</sup>. Hearing loss is often described as an inevitable decline which occurs during the ageing process<sup>(1,9)</sup>, however, emerging research suggests that potentially modifiable risk factors, including risk factors previously related to cardiovascular disease (CVD) risk<sup>(10,11)</sup>, may be associated with a decreased or increased risk of hearing loss. This has prompted investigation into the possibility that certain nutrients and foods may also be associated with incidence of hearing loss. Higher intakes of omega-3 fatty acids<sup>(10,12)</sup>, oily fish<sup>(10,12,13)</sup>, magnesium<sup>(14)</sup>, vitamin intake, including vitamins A<sup>(15)</sup>, B<sub>12</sub><sup>(16–18)</sup> C<sup>(14)</sup> and E<sup>(15)</sup>, antioxidant intake, including  $\beta$ -carotene<sup>(14)</sup>, and moderate alcohol consumption<sup>(19)</sup> have each been associated with a lower incidence of hearing loss. Conversely, Shargorodsky et al. (2010) found that overall intakes of vitamin C, E and  $\beta$ -carotene were not associated with the incidence of hearing loss in men<sup>(20)</sup>. Additionally, a high cholesterol intake<sup>(21)</sup>, a high consumption of foods with a high glycemic load<sup>(22)</sup> and excessive alcohol consumption<sup>(23)</sup> have been associated with an increased incidence of hearing loss. However, some of these studies have used only self-reported measures of hearing loss rather than objective measures which are preferable in this context<sup>(20,24,25)</sup>. Since associations have been reported between the above dietary factors and hearing loss, it seems plausible that certain dietary patterns (DPs) may also be associated with hearing loss.

In recent years, DP analysis has become a widely used method of investigating the relationship between diet and disease<sup>(26)</sup>. This technique adopts a holistic approach of examining diet and can be a useful complementary approach when examining specific individual nutrients, to more effectively capture the interaction between various nutrients<sup>(26,27)</sup>. Two main types of DP analysis can be carried out; *a priori* and *a posteriori*

methods. *A priori* methods include dietary indices, such as the Mediterranean Diet Score, which are based on nutritional recommendations and guidelines<sup>(28)</sup>, whilst *a posteriori* methods use multivariate statistical techniques such as factor analysis, principal component analysis (PCA) and cluster analysis<sup>(26)</sup> to derive the patterns within the dietary data<sup>(28)</sup>. For this analysis, PCA was performed to derive *a posteriori* DPs.

To the best of our knowledge, there have been no previous studies which have examined *a posteriori* DPs in relation to hearing loss. Spankovich et al. carried out *a priori* analysis and examined the Healthy Eating Index in relation to audiological thresholds, demonstrating an association between a healthy eating pattern and lower high frequency thresholds in adults aged 20-69 years old<sup>(29)</sup>. However, *a posteriori* analysis may hold some advantages over *a priori* analysis, in that this approach is data driven and does not rely on scientific guidelines or nutritional recommendations<sup>(30)</sup>. The *a posteriori* approach gives a true representation of what the DPs of a given population actually are, however, the DPs only represent the cohort they were derived from and may not be generalisable to other populations. In this study, we investigated the association between *a posteriori* DPs and hearing loss in men aged 45-59 years old enrolled in the Caerphilly Prospective Study (CaPS)<sup>(31)</sup>. Prevalence of hearing loss was carried out 5 years after dietary assessment. We hypothesised that a healthier DP would be associated with a reduced prevalence of hearing loss.

## SUBJECTS AND METHODS

### Study population

CaPS began recruitment between 1979 and 1983 (baseline). The original cohort consisted of 2,512 men who were aged between 45 and 59 years and lived in Caerphilly, or the

surrounding villages in Wales, United Kingdom. No exclusion criteria were applied. Subsequent examinations took place at five year intervals<sup>(32)</sup>. At phase 2, 561 men were lost to follow-up, therefore, an additional 447 men were included in the study, giving a new total of 2,398 men<sup>(33)</sup>. The initial aims of the study were to investigate ischaemic heart disease and the associations with various factors including cholesterol, fibrinogen, plasma viscosity, testosterone and insulin<sup>(34)</sup>. The baseline sample of 2,512 men were the focus of this study.

## **Ethics**

All CaPS participants gave written informed consent and the study had the approval of the local research ethics committee and adhered to the guidelines contained within the Declaration of Helsinki of 1975 as revised in 1983.

## **Dietary data**

A self-administered, semi-quantitative 56-item food-frequency questionnaire (FFQ) was completed during baseline examination<sup>(35)</sup>. The FFQ measured usual consumption of a range of foods. Frequency and quantity of intake of breads, fats, dairy products, sugar, alcohol, coffee and tea were asked for. For some of these foods, such as fats, dairy products and sugar, average intake per week for the family was requested. For such items, in order to estimate individual intake, the family intake stated for the FFQ was divided by a 'total family score'. To obtain this score, an adult or toddler aged 5 years or older was assigned a value of 1, a child aged between 1 and 4 years old was given a value of 0.5, and an infant under the age of 1 year was assigned a value of 0 as their contribution to the family intake was assumed to be negligible<sup>(35)</sup>. Frequency alone was measured for cereals, fruits, vegetables, eggs, meat, fish, confectionery and drinks. A 30% subsample of the men also completed a 7-day weighed food

intake (WI) to validate the FFQ as a more robust measure of dietary intake<sup>(35)</sup>. Pearson correlation coefficients were 0.3-0.4 across food items (alcohol 0.75), representing weak but statistically significant correlations<sup>(35)</sup>. Of the 764 men who completed the WI, only 665 men (87%) had maintained a satisfactory record and were included in this analysis<sup>(36)</sup>. FFQ data were available for the full cohort (2,512 men) and WI data were available for 665 men.

### **Auditory assessment**

Pure-tone unaided binaural threshold (dB<sub>A</sub>) was assessed at 4 different frequencies (0.5, 1, 2 and 4 kHz) with a Bosch audiometer and sound-reducing cups during the second phase, 5 years after baseline examination. Audiometric assessment was performed in a community clinic environment where background ambient noise was approximately 50 dB<sub>A</sub><sup>(37)</sup>. Assessment began at 0.5 kHz and 50 dB<sub>A</sub>. The sound level was decreased by 10 dB<sub>A</sub> until the sound could no longer be detected and the sound was then increased and decreased by 5 dB<sub>A</sub> until a threshold level was found. This technique was repeated for the other frequencies<sup>(37)</sup>. The pure-tone average (PTA) threshold was calculated as the average of the 4 frequencies (0.5, 1, 2 and 4 kHz) and both ears. Hearing loss was defined as PTA<sub>0.5-4kHz</sub> > 25 decibels (dB)<sup>(37)</sup>. Audiometric data were available for 1,886 men.

### **Assessment of covariates**

Anthropometry measures, including height and weight, were measured using a Holtain stadiometer, and a beam balance, respectively. Blood pressure was recorded by one observer using a Hawksley random zero mercury sphygmomanometer and a full 12-lead electrocardiogram was performed and Minnesota-coded by two experienced readers. The men

were invited to attend a clinic the following morning, after fasting overnight, to obtain a venous blood sample from which blood cholesterol was assessed<sup>(38)</sup>. Physical activity at work was estimated using the Health Insurance Plan questionnaire, and leisure time activity was assessed using the Minnesota Leisure Time Activity questionnaire. For the current analysis, a Physical activity Level (PAL) score was calculated by summing up activity levels at work, activity levels getting to and from work and leisure time physical activity. Two points were awarded if very active at work, one point was given if occasionally active at work, one point was given if one or more miles were travelled to work through cycling or walking, and one point was scored if consistent leisure activity was completed<sup>(39)</sup>. Participants were classified as non-smokers, ex-smokers, or current smoking, which included pipe or cigar smokers, light cigarette smokers (<15 per day), moderate cigarette smokers (15-24 per day) or heavy cigarette smokers ( $\geq 25$  per day). Social class was determined according to occupation; manual or non-manual, according to the Classification of occupations and coding index (1980)<sup>(40,41)</sup>.

## **Statistical analysis**

SPSS Statistics for Windows version 20 (IBM Corp., Armonk, NY) was used for all statistical analyses, including t-tests, chi-square tests, logistic and ordinal logistic regression models and PCA. All variables were normally distributed. To carry out PCA, all food and drink items in the FFQ and WI separately were condensed into 32 groups (Supplemental Table 1). In the initial stages of data analysis, to decide which method would give more accurate results, the WI food items were condensed into the same 32 food groups as the FFQ food items, but also into 43 food groups, as the WI comprised a larger number of food items. However, it was decided to condense the WI food items into the same 32 food groups as the FFQ items for ease of comparison of DPs and as a validation of the FFQ.



The process of PCA aggregates food items/groups according to how well they correlate with one another. The decision of how many factors to retain in the analysis was made by examining the break in the scree plot, along with Eigenvalues greater than one and the interpretability of the factors obtained. Orthogonal varimax rotation was then used to create a simpler structure with greater interpretability<sup>(42)</sup>. The DPs generated were then named according to the positive and negative factor loadings of food and drink items. Factor loadings  $<-0.2$  in magnitude were considered low and factor loadings  $>0.2$  in magnitude were considered high, and aided naming of the patterns.

Multiple logistic and ordinal logistic regression models were used to examine associations between the DPs with hearing loss. DPs were divided into fifths and each participant received a quintile ranking for each of the three DPs. Hearing loss was first assessed as a dichotomous variable with a cut point of  $>25$ dB PTA threshold to compare hearing loss with no hearing loss ( $\leq 25$ dB PTA threshold), and examined using logistic regression. Hearing loss was also assessed as an ordinal variable according to the categories; no hearing loss  $\leq 25$  dB HL, mild  $>25-40$  dB HL, moderate  $>40-60$  dB HL and severe hearing loss  $>60$  dB HL, and examined using ordinal logistic regression.

The models were adjusted for potential confounding factors. These included factors associated with both hearing loss and DPs in the current dataset. This was assessed by linear regression analysis. Other possible confounders from the current literature were also considered. The models were first adjusted for age (Model 1), then further adjusted for occupation (Model 2) (in the form of social class; manual or non-manual <sup>(37)</sup>), and then further adjusted for the continuous variables; body mass index (BMI), systolic blood pressure (SBP), physical activity level (PAL) score, total cholesterol and the categorical variable; smoking (non-smokers, ex-smokers, pipe or cigar smokers, light cigarette smokers, moderate cigarette smokers or heavy cigarette smokers) (Model 3). Other models were investigated,

including adjustment for age, occupation, smoking and PAL score, as it is possible the other variables may be intermediate markers rather than confounders, however, effect sizes were similar, therefore, the model proposed above (Model 3) was maintained. Height was also explored as a possible confounder, but did not significantly influence the models and therefore was not considered further. For the WI data, further adjustment for energy intake was explored but did not significantly affect the models, therefore data are not presented. Statistical significance was defined as  $P < 0.05$ .

## RESULTS

Baseline characteristics of all 2,512 men recruited for CaPS are shown in **Table 1**. The men were also grouped into two categories; those with hearing loss ( $PTA > 25\text{dB}$ ) and those with no hearing loss ( $\leq 25\text{dB}$  PTA) (**Table 1**). Compared with men without hearing loss, men with hearing loss were significantly older, shorter and lighter and were more likely to be current smokers and manual workers. Those with hearing loss and those with no hearing loss had similar BMIs, PAL score and total cholesterol levels.

Three DPs were determined by PCA using the FFQ data - Traditional, Healthy, High sugar/Low alcohol. Together, these three DPs explained 23.4% of the total variance. The Traditional pattern had high factor loading scores for the following foods: red meat, vegetables, processed meat, whitefish/shellfish, eggs, organ meat, poultry, lard, butter, potato, cheese, milk, oily fish, grains, fried potato, beer, sugar, tap water, soft drinks, tea and confectionery. The Healthy pattern was characterised by high positive loadings for cereals, fruit, high fibre bread, confectionery, vegetables, natural juices, margarine, milk and cream and negative loadings for beer, lard and butter. The High sugar/Low alcohol pattern had high factor loading scores for tea, sugar, milk, white bread, confectionery, fried potato and

negative loadings for wine, other alcoholic drinks, coffee, natural juices, high fibre bread and beer (Supplemental Table 2).

Logistic regression analysis of the FFQ data, using a cut-point of 25 dB for hearing loss, showed a protective effect for the Healthy DP after adjustment for age (OR per fifth=0.78, 95% CI= 0.73, 0.83,  $P < 0.001$ ) and a detrimental effect for the High sugar/Low alcohol pattern model (OR per fifth=1.12, 95% CI= 1.05, 1.20,  $P = 0.001$ ). The former association was hardly altered after adjustment for potential confounding factors (OR per fifth =0.83; 95% CI= 0.77, 0.90;  $p < 0.001$ ), but was consistent with chance variability for the High sugar/Low alcohol pattern as this association became insignificant ( $p = 0.16$ ) (**Table 2**). Similarly, only the Healthy DP remained significantly inversely associated with hearing loss after adjustment for potential confounding factors in the ordinal logistic regression analysis of the FFQ data (OR per fifth=0.87, 95% CI= 0.81, 0.94,  $P < 0.001$ ) (**Table 3**).

For the ordinal logistic regression, the categories of hearing loss were; no hearing loss  $\leq 25$  dB HL, mild  $> 25 - 40$  dB HL, moderate  $> 40 - 60$  dB HL and severe  $> 60$  dB HL. Data are presented with odds ratios of having greater hearing loss (reference; severe hearing loss) for those in each quintile of DP (reference; Q1). The odds ratio as a trend are also presented which represent a one increase in hearing loss category for each higher quintile of DP.

Three similar DPs were determined using factor analysis with the WI data- Traditional, Healthy, High sugar/Low alcohol. Together, these three DPs explained 20.2% of the total variance. The Traditional pattern was characterised by high loadings for butter, white bread, lard, sugar, tea, potatoes, red meat and eggs and negative loadings for cooking oil, high fibre bread, cereals and fruit juices. The Healthy pattern had high factor loadings for fruit, wine, confectionery, vegetables, other soft drinks, fruit juices, cheese, high fibre bread, other alcoholic drinks, cream, coffee and red meat and negative loadings for white bread, tea, sugar and cooking oil. The High sugar/Low alcohol pattern was characterised by high factor

loadings for milk, cereals, tea, confectionery, cream and sugar and negative loadings for beer, organ meat, eggs, red meat, potatoes fried, coffee, oily fish and lard (Supplemental Table 3).

After adjustment for potential confounding factors using the WI data, logistic regression analysis demonstrated a significant association between the Traditional pattern and greater risk of hearing loss (OR per fifth=1.18; 95% CI= 1.02, 1.35; P=0.02) and between the Healthy pattern and reduced risk of hearing loss (OR per fifth=0.85; 95% CI= 0.73, 0.99; P=0.03) (**Table 4**). Ordinal logistic regression analysis of the WI data showed that the Traditional DP remained significantly associated with hearing loss after adjustment for potential confounding factors (OR per fifth=1.17, 95% CI= 1.03, 1.33, P =0.02). The Healthy DP only just lost statistical significance once the model was fully adjusted (OR per fifth=0.87, 95% CI= 0.76, 1.00, P=0.06) (**Table 5**).

**Table 6** provides a summary of the results of the logistic and ordinal logistic regression analyses using both FFQ and WI data. This table shows that for the Healthy DP, three out of four analyses showed a statistically significant inverse association with hearing loss, whereas the Traditional DP demonstrated a significant positive association with hearing loss in two out of four analyses. The High sugar/Low alcohol DP was not significantly associated with hearing loss in any analyses in the fully adjusted models.

## DISCUSSION

The main finding from this study was that a Healthy DP was significantly inversely associated with prevalence of hearing loss. This was found using hearing loss as a dichotomous variable (cut-point of 25dB) for both FFQ and WI data, and using hearing loss as an ordinal variable (no hearing loss  $\leq$ 25 dB HL, mild >25 – 40 dB HL, moderate >40-60 dB HL, severe >60 dB HL) for the FFQ data, with the WI Healthy DP only just losing statistical significance (p=0.06). Prevalence of hearing loss was assessed 5 years after dietary

assessment, however, the findings presented are cross-sectional, therefore, the possibility of reverse causality cannot be discounted.

There was limited evidence showing that a Traditional DP was associated with an increased prevalence of hearing loss using logistic and ordinal logistic regression analyses of the WI data, but not with the FFQ data. The High sugar/Low alcohol DP was significantly associated with hearing loss in age-adjusted models for both logistic and ordinal logistic regression analyses of the FFQ data, but after further adjustment, this statistical significance was lost.

Very few studies have investigated DPs and hearing loss previously. Spankovich et al. (2013), investigated the Healthy Eating Index and hearing loss, and found that a more healthy diet was associated with better hearing at high frequencies in adults aged 20-69 years old<sup>(29)</sup>. Diet quality has also been examined in relation to concurrent vision and hearing impairment. Individuals in the lowest quintile compared to the highest quintile of dietary score had double the risk of having concurrent vision and hearing impairment<sup>(43)</sup>. To our knowledge, *a posteriori* DPs have not previously been examined in relation to hearing loss.

A greater number of studies have demonstrated significant associations between dietary factors and hearing loss. A diet high in oily fish<sup>(10,12,13)</sup>, omega-3 fatty acids<sup>(10,12)</sup>, vitamins and antioxidants<sup>(14,16-18,24)</sup> and moderate alcohol consumption<sup>(19)</sup> has been associated with a reduced risk of hearing loss, which supports our finding that a healthier diet is associated with reduced risk of hearing loss. Conversely, a high cholesterol intake<sup>(21)</sup> and a high intake of foods with a high glycemic load<sup>(22)</sup> have been associated with an increased risk of hearing loss.

Our study has examined DPs in relation to hearing loss and not only individual dietary factors. Examining individual nutrients or foods may not be optimal, due to the interaction

between nutrients. DP analysis, on the other hand, investigates the synergistic effects of nutrients and foods, producing a more comprehensive approach of examining overall diet<sup>(27)</sup>. DPs may be more likely to produce a significant association with risk of morbidity when compared with single nutrients<sup>(27)</sup>. Also, since fewer statistical tests are carried out in DP analysis, there is a smaller likelihood of obtaining results due to chance (type I error)<sup>(27)</sup>.

There is the possibility that the associations found between dietary factors and hearing loss are due in some part to the association between CVD risk factors and age-related hearing loss<sup>(11,45,46)</sup>. Elevated triglyceride levels, elevated resting heart rate, low level of high density lipoprotein cholesterol, high SBP, a history of smoking and increased BMI have been associated with an increased risk of hearing loss<sup>(11,44-47)</sup>. It has been hypothesised that the link between CVD risk factors and hearing loss may be due to reduced blood flow to the cochlea of the inner ear, which will reduce the ability to hear optimally<sup>(11)</sup>. Since the above studies<sup>(11,44-47)</sup> have shown that there could be a link between CVD risk factors and hearing loss, there is the possibility that certain dietary changes, which are likely to reduce CVD risk, may also have a beneficial influence on hearing loss.

Key strengths of our investigation include its large cohort size of 2,512 men. Also, although a FFQ was used to obtain dietary data from the full cohort, a 7-day WI was also completed in a 30% subset. This robust dietary assessment method is unusual in epidemiological studies. In a previous validation study of the FFQ using the WI, Pearson correlation coefficients were 0.3-0.4 across food items (alcohol 0.75), representing weak but statistically significant correlations<sup>(35)</sup>. Furthermore, hearing loss was measured using audiometry, in contrast to many other studies which have only used self-reported measures<sup>(20,24,25)</sup>.

Nevertheless, there are several limitations to consider. Only men were investigated in the study and these men were all living in the town of Caerphilly, or surrounding villages in

Wales, therefore, the generalizability of the results of this study to the wider population may be limited. Further limitations were that men with conductive hearing loss, otosclerosis etc. were not excluded from the analysis, information on hearing-aid use was not collected and information was not available on individuals who were lost to follow-up.

The FFQ was also limited for some food groups, particularly for fruit. This may have resulted in some measurement error in the DPs found from the FFQ<sup>(48)</sup>. The weighed intake also has some negatives as people may change their dietary habits when they know they are weighing their food and assessing their dietary intake. Also, auditory assessment was not conducted in an optimal setting (i.e. in a soundproof booth), but the technique used was validated in 70 participants with full clinical assessment using a sound proof booth. Good correlations were found between procedures at each of the four frequencies ( $r=0.69-0.93$ )<sup>(37)</sup>. The DP analysis was conducted in the full cohort of 2,512 men, whilst audiometric assessment was only carried out in 1,886 men. Ideally, the DP analysis would be carried out only in those with audiometric assessment.

Furthermore, although adjustment was made for numerous potential confounding factors, there is still the possibility of residual confounding. In particular, exposure to noise, socioeconomic status and CVD risk factors may not have been fully accounted for. Information on chronic conditions such as heart disease, stroke, diabetes, hypertension were collected, however, we did not have access to these data for the current analysis. Occupation (in the form of social class) was adjusted for, which would have accounted for some workplace noise exposure, as well as socioeconomic status. There is, however, a possibility of residual confounding by exposure to noise as part of employment not accounted for by the social class variable. Several CVD risk factors were also adjusted for, however, these factors may not have been fully accounted for in the current analysis. We determined which factors were associated with both hearing loss and DPs to ensure that true confounding factors were

adjusted for, and we adjusted for similar potential confounding factors which have been previously used in the literature when examining diet and hearing loss<sup>(10,14,15,20,49)</sup>. Various models were investigated further since it is possible that BMI, SBP and total cholesterol could actually be intermediate markers rather than confounders, and that we have therefore over-adjusted the models. A model of adjustment for age, occupation, smoking and PAL score was also investigated, excluding possible intermediate markers, however effect sizes were very similar. Height was also explored in the models as a factor which cannot be affected by recent dietary intake, whereas BMI can, however, this did not greatly influence the models, and therefore was not included in any further analyses.

DP analysis can also be relatively subjective and a number of arbitrary decisions were made, including how to best group food items into food groups, the number of patterns to be kept for the final analysis and the naming of the identified patterns<sup>(42,48)</sup>. As an example, we decided to maintain several alcoholic beverages groups, instead of merging them together, since health benefits of alcohol beverages have been suggested to differ depending on the type of beverage and associated pattern of consumption, therefore, we kept these groups separate as we were interested in determining whether these might affect the produced dietary patterns.

An advantage of our analysis is the use of both FFQ and WI data, which produced similar DPs. Spearman's correlation coefficients between the DPs found using the FFQ and the WI ranged from 0.32 for the Traditional patterns and Healthy patterns, to 0.4 for the correlation between the High sugar/Low alcohol patterns, which indicated a fairly weak to moderate but statistically significant correlation.

A recent study which carried out DP analysis in the same CaPS cohort as in this study found some similarities, but also some differences<sup>(33)</sup>. They did not name their patterns.



Indeed, it was difficult to name the DPs in this study, which is one of the limitations of *a posteriori* DP analysis<sup>(48)</sup>. Mertens et al. (2017) found a mainly similar traditional pattern as in our study. Their second DP was different with a high intake of pulses, as well as meat, fish, rice, pasta, fruit, vegetables and eggs. Our healthy pattern was similar in some ways with high factor loadings for cereals, vegetables and fruit. There was also a similar third pattern which was characterised by confectionary and sweet foods, as well as avoidance of alcohol<sup>(33)</sup>. This analysis, however, differed from our analysis as they used dietary questionnaires from Phases 2 and 3 of the CAPS, which took place over a period of 5 years, to generate their DPs, hence similar DPs would not necessarily be expected<sup>(33)</sup>. A limitation of our study is the derivation of DPs from data which is over 40 years old, therefore, as found in the study by Mertens et al (2017), DPs will have changed since then<sup>(33)</sup>.

The issue of whether or not to adjust for energy intake in DP analysis is debatable<sup>(50,51)</sup>. Energy requirements vary according to age, gender, BMI and PALs, therefore, as overall food intake will differ by these factors, it is generally considered more appropriate to adjust for energy intake in analyses of dietary intake. Energy adjustment is required for a number of reasons; to control for confounding, to give a measure of dietary composition, not just dietary intake, and to mitigate the effects of measurement error<sup>(49,51)</sup>. In this current analysis, adjustment for energy intake of the WI data did not appreciably alter effect sizes. In previous studies, adjustment for energy intake did slightly alter factor loadings and derived DPs, but did not greatly alter the associations with variables such as birthweight<sup>(52,53)</sup>.

Furthermore, there is a relatively small amount of variance in dietary data explained by the three DPs. This could be perhaps due to other DPs also being present in this cohort. It was also not possible to measure change in diet or hearing loss as these were both only assessed once. This is a limitation particularly because auditory assessment was only assessed

once, 5 years after dietary assessment.

## **CONCLUSION**

Hearing loss can have a significant detrimental impact on a person's emotional health and can be very isolating and debilitating. We found that a Healthy DP was significantly and inversely associated with the prevalence of hearing loss in older men aged 45-59 years old in the Caerphilly Prospective Study. This demonstrates that a healthy diet may contribute to a reduced risk of hearing loss. However, the role of dietary factors in hearing loss remains to be fully established and warrants further investigation using robust exposure and endpoint assessment.

## **Authors' contributions to manuscript**

J. Y., J. G., Y. B. S. and A. F. designed research; J. Y., J. G., A. F. acquisition of data; N. G., C. P., C. N. and N. L. analysed data; N. G. wrote paper; C. N., C. P., J. Y., N. G., Y. B. S. and J. W. critical revision of manuscript; and N. G. and J. W. had primary responsibility for final content. All authors read and approved the final manuscript. Authors have no potential conflicts of interest.

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## Results Tables

TABLE 1

Baseline characteristics of all men aged 45-59 years in the Caerphilly Prospective Study grouped according to having hearing loss (PTA>25dB) or no hearing loss (PTA≤25dB).

Characteristic	Baseline Caerphilly participants			
	All participants	No hearing loss	Hearing loss	P value
	(n=2512)	(PTA≤25dB) (n=890)	(PTA>25dB) (n=996)	
Age (y); mean ± SD	52.1 ± 4.5	50.8 ± 4.2	53.0 ± 4.4	<0.001
Height (m); mean ± SD	1.71 ± 0.06	1.72 ± 0.06	1.70 ± 0.06	<0.001
Weight(kg); mean ± SD	76.6 ± 12.1	77.6 ± 11.4	76.0 ± 11.7	0.003
BMI (kg/m <sup>2</sup> ); mean ± SD	26.2 ± 3.6	26.2 ± 3.3	26.1 ± 3.6	0.49
Systolic blood pressure; mean ± SD	140.77 ± 19.35	139.31 ± 18.41	141.16 ± 19.56	0.04
Total cholesterol; mean ± SD	5.70 ± 1.14	5.72 ± 1.17	5.69 ± 1.08	0.57
Physical activity level (n (%)) with no physical activity)	501 (19.9)	152 (17.1)	160 (16.1)	0.15
Current smoker [n (%)]	1387 (56)	426 (48)	555 (56)	<0.001
Manual worker [n (%)]	1668 (68)	488 (56)	728 (74)	<0.001
Dietary pattern factor loading scores				
Traditional FFQ	0 (1)	-0.009 (0.83)	0.036 (0.97)	0.28
Healthy FFQ	0 (1)	0.256 (0.99)	-0.095 (0.97)	<0.001

<b>High sugar/Low alcohol FFQ</b>	0 (1)	-0.104 (1.04)	0.034 (0.97)	0.003
<b>Traditional WI</b>	0 (1)	-0.101 (1.07)	0.107 (0.95)	0.02
<b>Healthy WI</b>	0 (1)	0.182 (1.06)	-0.132 (0.90)	<0.001
<b>High sugar/Low alcohol WI</b>	0 (1)	-0.022 (0.90)	0.014 (1.01)	0.67

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Independent samples t-tests were used for continuous variables and chi-square tests for categorical variables.

N-value for WI data no hearing loss  $n_{\max}$  236 and hearing loss  $n_{\max}$  279; *PTA*, *pure-tone average*; *dB*, *decibel*.

**TABLE 2**

Logistic regression analysis of the association between hearing loss (PTA>25dB) and quintiles of dietary pattern factor score for FFQ data from the Caerphilly Prospective Study.

	<b>Dietary pattern</b>		
	<b>Traditional</b>	<b>Healthy</b>	<b>High sugar/Low alcohol</b>
	<b>OR (95%CI)<sup>1</sup></b>	<b>OR (95%CI)<sup>1</sup></b>	<b>OR (95%CI)<sup>1</sup></b>
<b>Model 1 - Adjustment for age</b>			
<b>Q1 (low pattern adherence; n<sub>max</sub>=503)</b>	1.00 (reference)	1.00 (reference)	1.00 (reference)
<b>Q2 (n<sub>max</sub>=503)</b>	1.15 (0.86, 1.53)	0.69 (0.51, 0.93)	1.14 (0.86, 1.53)
<b>Q3 (n<sub>max</sub>=503)</b>	1.01 (0.75, 1.35)	0.66 (0.49, 0.86)	1.52 (1.13, 2.04)
<b>Q4 (n<sub>max</sub>=503)</b>	1.35 (1.00, 1.82)	0.43 (0.32, 0.58)	1.26 (0.93, 1.69)
<b>Q5 (high pattern adherence; n<sub>max</sub>=503)</b>	1.14 (0.84, 1.53)	1.21 (0.89, 1.67)	0.89 (0.66, 1.19)
<b>Per fifth<sup>2</sup></b>	1.04 (0.97, 1.11)	0.78 (0.73, 0.83)	1.12 (1.05, 1.20)
<b>P value for trend</b>	0.31	<0.001	0.001
<b>Model 2 - Adjustment for age and occupation</b>			
<b>Q1 (n<sub>max</sub>=503)</b>	1.00 (reference)	1.00 (reference)	1.00 (reference)
<b>Q2 (n<sub>max</sub>=503)</b>	0.90 (0.66, 1.22)	0.89 (0.65, 1.22)	1.03 (0.76, 1.39)
<b>Q3 (n<sub>max</sub>=503)</b>	1.01 (0.75, 1.36)	0.63 (0.46, 0.87)	1.13 (0.84, 1.53)
<b>Q4 (n<sub>max</sub>=503)</b>	0.90 (0.67, 1.23)	0.67 (0.49, 0.92)	1.43 (1.05, 1.95)

<b>Q5 (n<sub>max</sub>=503)</b>	1.20 (0.88, 1.64)	0.46 (0.33, 0.63)	1.15 (0.84, 1.58)
<b>Per fifth<sup>2</sup></b>	1.04 (0.97, 1.1)	0.83 (0.77, 0.89)	1.06 (0.99, 1.14)
<b>P value for trend</b>	0.29	<0.001	0.08
<b>Model 3 - Adjustment for age, occupation, body mass index, systolic blood pressure, smoking, physical activity level and total cholesterol</b>			
<b>Q1 (n<sub>max</sub>=503)</b>	1.00 (reference)	1.00 (reference)	1.00 (reference)
<b>Q2 (n<sub>max</sub>=503)</b>	0.90 (0.65, 1.23)	0.89 (0.64, 1.24)	1.05 (0.77, 1.44)
<b>Q3 (n<sub>max</sub>=503)</b>	0.99 (0.72, 1.35)	0.64 (0.46, 0.88)	1.12 (0.82, 1.52)
<b>Q4 (n<sub>max</sub>=503)</b>	0.89 (0.65, 1.22)	0.70 (0.50, 0.97)	1.46 (1.06, 2.01)
<b>Q5 (n<sub>max</sub>=503)</b>	1.16 (0.84, 1.61)	0.45 (0.32, 0.64)	1.10 (0.79, 1.53)
<b>Per fifth<sup>2</sup></b>	1.03 (0.96, 1.11)	0.83 (0.77, 0.90)	1.06 (0.98, 1.14)
<b>P value for trend</b>	0.44	<0.001	0.16

Hearing loss defined as PTA>25dB.

<sup>1</sup> Odds ratio for hearing loss in comparison to Q1 (reference).

<sup>2</sup> Odds ratio for hearing loss per fifth of dietary pattern factor score

*Q*, fifth of dietary pattern factor score; *PTA*, pure-tone average; *dB*, decibel.

**TABLE 3**

Ordinal logistic regression analysis of the association between categories of hearing loss (no hearing loss  $\leq 25$  dB HL, mild  $>25 - 40$  dB HL, moderate  $>40-60$  dB HL, severe  $>60$  dB HL) and-quintiles of dietary pattern factor score for FFQ data from the Caerphilly Prospective Study.

	<b>Dietary pattern</b>		
	<b>Traditional</b>	<b>Healthy</b>	<b>High sugar/ Low alcohol</b>
	<b>OR (95%CI)<sup>1</sup></b>	<b>OR (95%CI)<sup>1</sup></b>	<b>OR (95%CI)<sup>1</sup></b>
<b>Model 1 - Adjustment for age</b>			
<b>Q1 (low pattern adherence; n<sub>max</sub>=503)</b>	1.00 (reference)	1.00 (reference)	1.00 (reference)
<b>Q2 (n<sub>max</sub>=503)</b>	0.90 (0.68, 1.19)	0.94 (0.71, 1.25)	1.08 (0.81, 1.43)
<b>Q3 (n<sub>max</sub>=503)</b>	1.04 (0.79, 1.38)	0.66 (0.50, 0.88)	1.28 (0.97, 1.70)
<b>Q4 (n<sub>max</sub>=503)</b>	0.93 (0.70, 1.23)	0.60 (0.45, 0.79)	1.72 (1.30, 2.27)
<b>Q5 (high pattern adherence; n<sub>max</sub>=503)</b>	1.24 (0.94, 1.65)	0.42 (0.32, 0.56)	1.38 (1.04, 1.83)
<b>Per fifth<sup>2</sup></b>	1.05 (0.98, 1.12)	0.80 (0.76, 0.86)	1.12 (1.05, 1.19)
<b>P value for trend</b>	0.14	<0.001	0.001
<b>Model 2 - Adjustment for age and occupation</b>			
<b>Q1 (n<sub>max</sub>=503)</b>	1.00 (reference)	1.00 (reference)	1.00 (reference)
<b>Q2 (n<sub>max</sub>=503)</b>	0.92 (0.70, 1.23)	1.05 (0.79, 1.39)	0.97 (0.73, 1.29)
<b>Q3 (n<sub>max</sub>=503)</b>	1.05 (0.80, 1.39)	0.76 (0.57, 1.00)	1.11 (0.84, 1.48)

<b>Q4 (n<sub>max</sub>=503)</b>	0.95 (0.72, 1.27)	0.77 (0.58, 1.02)	1.40 (1.05, 1.87)
<b>Q5 (n<sub>max</sub>=503)</b>	1.27 (0.96, 1.69)	0.56 (0.42, 0.75)	1.10 (0.82, 1.48)
<b>Per fifth<sup>2</sup></b>	1.05 (0.99, 1.12)	0.86 (0.81, 0.92)	1.06 (0.99, 1.13)
<b>P value for trend</b>	0.12	<0.001	0.08

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**Model 3 - Adjustment for age, occupation, body mass index, systolic blood pressure, smoking, physical activity level and total cholesterol**

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<b>Q1 (n<sub>max</sub>=503)</b>	1.00 (reference)	1.00 (reference)	1.00 (reference)
<b>Q2 (n<sub>max</sub>=503)</b>	0.92 (0.69, 1.23)	1.07 (0.79, 1.43)	0.99 (0.74, 1.33)
<b>Q3 (n<sub>max</sub>=503)</b>	1.03 (0.77, 1.37)	0.79 (0.59, 1.06)	1.09 (0.81, 1.46)
<b>Q4 (n<sub>max</sub>=503)</b>	0.95 (0.71, 1.27)	0.82 (0.61, 1.11)	1.45 (1.08, 1.95)
<b>Q5 (n<sub>max</sub>=503)</b>	1.23 (0.91, 1.65)	0.58 (0.42, 0.79)	1.06 (0.78, 1.44)
<b>Per fifth<sup>2</sup></b>	1.04 (0.98, 1.12)	0.87 (0.81, 0.94)	1.05 (0.98, 1.13)
<b>P value for trend</b>	0.20	<0.001	0.14

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Categories of hearing loss; no hearing loss  $\leq 25$  dB HL, mild  $>25 - 40$  dB HL, moderate  $>40-60$  dB HL, severe  $>60$  dB HL.

<sup>1</sup> Odds ratios of having greater hearing loss (reference; severe hearing loss) for those in each quintile of DP (reference; Q1).

<sup>2</sup> Odds ratio for a one increase in hearing loss category for each higher quintile of DP

*PTA, pure-tone average; dB, decibel.*

**TABLE 4**

Logistic regression analysis of the association between hearing loss (PTA>25dB) and quintiles of dietary pattern factor score for WI data from the Caerphilly Prospective Study.

	Dietary pattern		
	Traditional	Healthy	High sugar/ Low alcohol
	OR (95%CI) <sup>1</sup>	OR (95%CI) <sup>1</sup>	OR (95%CI) <sup>1</sup>
<b>Model 1 - Adjustment for age</b>			
<b>Q1 (low pattern adherence; n<sub>max</sub>=133)</b>	1.00 (reference)	1.00 (reference)	1.00 (reference)
<b>Q2 (n<sub>max</sub>=133)</b>	1.17 (0.67, 2.03)	0.80 (0.46, 1.39)	0.79 (0.45, 1.39)
<b>Q3 (n<sub>max</sub>=133)</b>	0.76 (0.43, 1.35)	0.70 (0.40, 1.22)	1.20 (0.68, 2.12)
<b>Q4 (n<sub>max</sub>=133)</b>	1.60 (0.92, 2.77)	0.42 (0.24, 0.74)	0.90 (0.51, 1.60)
<b>Q5 (high pattern adherence; n<sub>max</sub>=133)</b>	0.52 (0.29, 0.92)	0.97 (0.55, 1.72)	1.31 (0.74, 2.32)
<b>Per fifth<sup>2</sup></b>	1.22 (1.07, 1.38)	0.82 (0.72, 0.93)	0.94 (0.83, 1.07)
<b>P value for trend</b>	0.002	0.002	0.37
<b>Model 2 - Adjustment for age and occupation</b>			
<b>Q1 (n<sub>max</sub>=133)</b>	1.00 (reference)	1.00 (reference)	1.00 (reference)
<b>Q2 (n<sub>max</sub>=133)</b>	1.93 (1.07, 3.48)	1.16 (0.65, 2.09)	0.83 (0.46, 1.49)
<b>Q3 (n<sub>max</sub>=133)</b>	2.14 (1.19, 3.86)	0.97 (0.54, 1.74)	0.67 (0.38, 1.17)
<b>Q4 (n<sub>max</sub>=133)</b>	1.23 (0.67, 2.27)	0.90 (0.50, 1.62)	1.05 (0.59, 1.87)
	2.60 (1.43, 4.70)	0.55 (0.29, 1.01)	

<b>Q5 (n<sub>max</sub>=133)</b>			0.77 (0.43, 1.37)
<b>Per fifth<sup>2</sup></b>	1.16 (1.02, 1.32)	0.87 (0.76, 0.99)	0.97 (0.85, 1.11)
<b>P value for trend</b>	0.03	0.04	0.65
<b>Model 3 - Adjustment for age, occupation, body mass index, systolic blood pressure, smoking, physical activity level and total cholesterol</b>			
<b>Q1 (n<sub>max</sub>=133)</b>	1.00 (reference)	1.00 (reference)	1.00 (reference)
<b>Q2 (n<sub>max</sub>=133)</b>	1.89 (1.03, 3.47)	1.08 (0.58, 1.99)	0.86 (0.47, 1.59)
<b>Q3 (n<sub>max</sub>=133)</b>	2.17 (1.18, 4.01)	0.93 (0.50, 1.74)	0.71 (0.39, 1.28)
<b>Q4 (n<sub>max</sub>=133)</b>	1.30 (0.69, 2.46)	0.86 (0.46, 1.60)	0.92 (0.50, 1.68)
<b>Q5 (n<sub>max</sub>=133)</b>	2.67(1.43, 5.01)	0.490.25, 0.96)	0.85 (0.46, 1.56)
<b>Per fifth<sup>2</sup></b>	1.18 (1.02, 1.35)	0.85 (0.73, 0.99)	0.97 (0.85, 1.12)
<b>P value for trend</b>	0.02	0.03	0.69

Hearing loss defined as PTA>25dB.

<sup>1</sup> Odds ratio for hearing loss in comparison to Q1 (reference).

<sup>2</sup> Odds ratio for hearing loss per fifth of dietary pattern factor score

*PTA, pure-tone average; dB, decibel.*



**TABLE 5**

Ordinal logistic regression analysis of the association between categories of hearing loss (no hearing loss  $\leq 25$  dB HL, mild  $>25 - 40$  dB HL, moderate  $>40-60$  dB HL, severe  $>60$  dB HL) and quintiles of dietary pattern factor score for WI data from the Caerphilly Prospective Study.

	<b>Dietary pattern</b>		
	<b>Traditional</b>	<b>Healthy</b>	<b>High sugar/ Low alcohol</b>
	<b>OR (95%CI)<sup>1</sup></b>	<b>OR (95%CI)<sup>1</sup></b>	<b>OR (95%CI)<sup>1</sup></b>
<b>Model 1 - Adjustment for age</b>			
<b>Q1 (low pattern adherence; n<sub>max</sub>=133)</b>	1.00 (reference)	1.00 (reference)	1.00 (reference)
<b>Q2 (n<sub>max</sub>=133)</b>	2.09 (1.21, 3.62)	0.81 (0.47, 1.37)	0.77 (0.45, 1.32)
<b>Q3 (n<sub>max</sub>=133)</b>	2.03 (1.17, 3.51)	0.82 (0.49, 1.39)	0.61 (0.37, 1.03)
<b>Q4 (n<sub>max</sub>=133)</b>	1.53 (0.86, 2.70)	0.60 (0.35, 1.03)	0.82 (0.48, 1.37)
<b>Q5 (high pattern adherence; n<sub>max</sub>=133)</b>	3.14 (1.82, 5.43)	0.45 (0.26, 0.77)	0.66 (0.39, 1.12)
<b>Per fifth<sup>2</sup></b>	1.22 (1.08, 1.37)	0.83 (0.73, 0.94)	0.92 (0.82, 1.04)
<b>P value for trend</b>	0.001	0.002	0.19
<b>Model 2 - Adjustment for age and occupation</b>			
<b>Q1 (n<sub>max</sub>=133)</b>	1.00 (reference)	1.00 (reference)	1.00 (reference)
<b>Q2 (n<sub>max</sub>=133)</b>	2.09 (1.20, 3.66)	0.87 (0.51, 1.49)	0.81 (0.47, 1.40)
<b>Q3 (n<sub>max</sub>=133)</b>	1.93 (1.10, 3.39)	0.98 (0.57, 1.67)	0.67 (0.39, 1.13)

<b>Q4 (n<sub>max</sub>=133)</b>	1.30 (0.72, 2.34)	0.72 (0.42, 1.25)	0.91 (0.53, 1.54)
<b>Q5 (n<sub>max</sub>=133)</b>	2.68 (1.53, 4.68)	0.57 (0.32, 1.02)	0.73 (0.43, 1.25)
<b>Per fifth<sup>2</sup></b>	1.17 (1.03, 1.32)	0.88 (0.78, 1.00)	0.95 (0.84, 1.07)
<b>P value for trend</b>	0.02	0.06	0.40

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**Model 3 - Adjustment for age, occupation, body mass index, systolic blood pressure, smoking, physical activity level and total cholesterol**

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<b>Q1 (n<sub>max</sub>=133)</b>	1.00 (reference)	1.00 (reference)	1.00 (reference)
<b>Q2 (n<sub>max</sub>=133)</b>	2.04 (1.15, 3.62)	0.81 (0.47, 1.42)	0.82 (0.47, 1.44)
<b>Q3 (n<sub>max</sub>=133)</b>	1.98 (1.11, 3.53)	0.99 (0.56, 1.74)	0.69 (0.40, 1.20)
<b>Q4 (n<sub>max</sub>=133)</b>	1.36 (0.74, 2.50)	0.68 (0.38, 1.22)	0.77 (0.44, 1.35)
<b>Q5 (n<sub>max</sub>=133)</b>	2.68 (1.50, 4.79)	0.55 (0.30, 1.02)	0.78 (0.44, 1.37)
<b>Per fifth<sup>2</sup></b>	1.17 (1.03, 1.33)	0.87 (0.76, 1.00)	0.94 (0.83, 1.07)
<b>P value for trend</b>	0.02	0.06	0.37

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Categories of hearing loss; no hearing loss  $\leq 25$  dB HL, mild  $>25 - 40$  dB HL, moderate  $>40-60$  dB HL, severe  $>60$  dB HL.

<sup>1</sup> Odds ratios of having greater hearing loss (reference; severe hearing loss) for those in each quintile of DP (reference; Q1).

<sup>2</sup> Odds ratio for a one increase in hearing loss category for each higher quintile of DP

*PTA, pure-tone average; dB, decibel.*

**TABLE 6**

Summary table of logistic and ordinal logistic regression analyses of the association between hearing loss (PTA>25dB for logistic regression and categories of hearing loss; no hearing loss ≤25 dB HL, mild >25 – 40 dB HL, moderate >40-60 dB HL and severe >60 dB HL for ordinal logistic regression) and quintiles of dietary pattern factor score (Q1-Q5) after full adjustment for potential confounding factors<sup>1</sup> for FFQ and WI data from the Caerphilly Prospective Study.

	Dietary pattern					
	Traditional FFQ	Traditional WI	Healthy FFQ	Healthy WI	High sugar/ Low alcohol FFQ	High sugar/ Low alcohol WI
<b>Logistic regression (HL-PTA&gt;25 dB)<sup>2</sup></b>						
<b>OR per fifth (95%CI)<sup>3</sup></b>	1.03 (0.96, 1.11)	1.18 (1.02, 1.35)	0.83 (0.77, 0.90)	0.85 (0.73, 0.99)	1.06 (0.98, 1.14)	0.97 (0.85, 1.12)
<b>P value</b>	0.44	0.02	<0.001	0.03	0.16	0.69
<b>Ordinal logistic regression (HL-PTA&gt;25 dB)<sup>4</sup></b>						
<b>OR per fifth (95%CI)<sup>3</sup></b>	1.04 (0.98, 1.12)	1.17 (1.03, 1.33)	0.87 (0.81, 0.94)	0.87 (0.76, 1.00)	1.05 (0.98, 1.13)	0.94 (0.83, 1.07)
<b>P value for trend</b>	0.20	0.02	<0.001	0.06	0.14	0.37

<sup>1</sup>Adjustment for age, occupation, body mass index, systolic blood pressure, smoking, physical activity level and total cholesterol.

<sup>2</sup>Hearing loss defined as PTA>25dB for logistic regression.

<sup>3</sup>OR, Odds ratio for hearing loss per fifth of dietary pattern factor score

<sup>4</sup>Categories of hearing loss; no hearing loss  $\leq 25$  dB HL, mild  $>25 - 40$  dB HL, moderate  $>40-60$  dB HL, severe  $>60$  dB HL.

*PTA, pure-tone average; dB, decibel.*