The association between diet and blood pressure in UK adolescents: using current data and new technologies

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The candidate confirms that the work submitted is her own and that appropriate credit has been given where reference has been made to the work of others.

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Abstract

Background

Hypertension is one of the leading risk factors to health. Although the burden of hypertension is concentrated in older populations, it is now recognised that the origins of hypertension are rooted in the early stage of life. Elevated blood pressure in youth is a strong predictor of hypertension in adulthood. Previous studies found that life style factors, for example diet, can affect blood pressure status, but relevant studies in adolescents are lacking.

Carrying out epidemiology research online rather than using traditional face-to-face methods is becoming a novel method worth studying. These new methods, including recruiting participants through social network websites, completing questionnaire or dietary record online, etc., will allow researchers to obtain sample in a wider geographic area with lower costs in time and money, are more convenient and are more acceptable for participants to collect sensitive information.

Aims and objectives

The aims of the study it to develop a pilot online research method to explore the association between diet and blood pressure in adolescents. There are two main objectives: a) to find out key dietary factors that may affects blood pressure levels in adolescents using existing data, and b) to explore the feasibility of use new technology (for example online recruitment, online questionnaire, online dietary record, blood pressure measurements, etc.) in epidemiology studies.

Methods

Existing data was used to analyse the association between diet and blood pressure in 10 to 19 years old adolescents. National Diet and Nutrition Survey (NDNS) dataset was used as cross-sectional data, and Avon Longitudinal Study of Parents and Children (ALSPAC) dataset was used as longitudinal data. Data was cleaned and transformed. Linear regression, logistic regression and survival analysis were used to explain the association between diet and blood pressure levels.

The Online Research of Adolescents and Good Eating Study (ORANGE Study) was set up to explore the feasibility of online survey. It included two stages:

School-based stage: 13 to 19 years old participants were recruited from local school students, visiting students on university open-days and first year students in the University of Leeds. Questionnaires were used to find out the adolescents' attitude to an online health research. How willingly they were to click on the advert and take part an online health research, which factor would affect their attitude were asked in the questionnaire. The accuracy of self-measured blood pressure values using a self-designed instruction was also tested in this stage.

Web-based stage: 579 participants were recruited through social network websites (Facebook and Instagram). Fifty participants were randomly selected to complete the whole study. They received blood pressure measuring tools by post. They were then asked to measure their own blood pressure, complete an online questionnaire and a 3-day online dietary record. The following factors were calculated and compared to those of the school-based stage to evaluate the feasibility of online survey: response rates, completion rates, time and money expenditure and sample characters.

Results and conclusion

7%~10% of the adolescents were hypertensive in NDNS and ALSPAC population. Dietary vitamin E intake was linked with lower blood pressure levels in cross-sectional dataset, but not in longitudinal dataset. Dietary fat intake was linked with higher blood pressure levels in both cross-sectional dataset and longitudinal dataset.

Self-measured blood pressure of the adolescents showed acceptable accuracy when comparing to standard blood pressure values that measured by the researchers. In the ORANGE study, 89% of the participants used Facebook in the last week, 21% of the participants would like to click on the advert of online survey, and 32% of the participants would like to take part in the survey. In the pilot online study, response rate of the web-based sample was a bit higher than school-based stage. Compared with traditional school-based study, the time expenditure per valid participants on the web-based study is less, but the money expenditure is higher. Compared with national data (NDNS population), in both school-based stage and web-based stage, fewer participants under 16 years were recruited, fewer male participants were recruited, and more white participants were recruited. In summary, the web-based study expensed more money but less time, and the sample recruited is no worse than that in school-based sample.

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Abbreviation

American Academy of Pediatrics	AAP
Ambulatory blood pressure monitoring	ABPM
Acquired immune deficiency syndrome	AIDS
Avon Longitudinal Study of Parents and Children	ALSPAC
Body Mass Index	BMI
Blood pressure	BP
Computer Assisted Personal interview	CAPI
Coronary heart disease	CHD
Confidence interval	CI
Directed Acyclic Graph	DAG
Disability-adjusted life years	DALY
Diastolic blood pressure	DBP
Diastolic blood pressure Z-score	DBPZ
Docosahexaenoic acid	DHA
Food Frequency Questionnaire	FFQ
fruit and vegetable intake	FVI
Global Burden of Disease Study 2010	GBD 2010
Glycemic index	GI
Glycemic load	GL
High density lipoprotein	HDL
Human immunodeficiency virus	HIV
United States National Health and Nutrition Examination Survey	HNANES
Hazard ratio	HR
Ischemic heart disease	IHD
Korea School Health Examination Survey	KSHES
Low density lipoprotein	LDL
Monounsaturated fatty acid	MUFA
National Dietary and Nutrition Survey	NDNS
The Organization for Economic Co-operation and Development	OECD
Odds ratio	OR
The Online Research of Adolescents and Good Eating Study	ORANGE Study

Personal computer	PC
protein kinase	PKC
Prospective Studies Collaboration	PSC
Polyunsaturated fatty acid	PUFA
reactive oxygen species	ROS
Systolic blood pressure	SBP
Systolic blood pressure Z-score	SBPZ
Standard Deviation	SD
Standard Deviation Score	SDS
Saturated fatty acid	SFA
Sugar-sweetened beverages	SSB
Trans fatty acid	TFA
The United Kingdom	UK
United Nations Children's Fund	UNICEF
The World Health Organization	WHO

Chapter 1. Introduction and literature review: dietary factors and blood pressure in adolescents

1.1 Introduction

1.1.1 Adolescents health

According to the United Nations Children's Fund (UNICEF) data, there are around 1.2 billion adolescents aged 10 to 19 years, making up 16 percent of the world's population in the year of 2016 (Unicef, 2016). Adolescence is one of the most rapid phases of human development. The changes in adolescents' health may have consequence affect over their whole life-course. Nearly 35% of the global burden of disease has roots in adolescence (WHO, 2018d).

Adolescence is a period of both risk and opportunity. The majority of adolescents are considered healthy, the mortality rates are low in this age group compared with other age groups (WHO, 2018a). Road injuries, acquired immune deficiency syndrome (AIDS) -related causes, suicide, lower respiratory infections and interpersonal violence were the top five leading causes of death. In 2012, an estimated 1.3 million adolescents died. Forty three percent of the death was in the Africa Region and twenty seven percent was in the South-East Asia Region. Depression, road injuries, iron deficiency anaemia, human immunodeficiency virus (HIV) and suicide are the major causes of disability-adjusted life years (DALY) lost in 10–19 year olds (Unicef, 2016). Besides these leading factors, early pregnancy and childbirth, using of alcohol, tobacco and drug, obesity, exercise and nutrition are also health issues that influence the well-being of adolescents (WHO, 2018b).

The unique nature and importance of adolescence implicates that policy and research to explore and improve their health condition should take place among adolescents (WHO, 2014b). Four core areas to action in for the health sections in each country were suggested by the World Health Organization (WHO):

- providing health services
- collecting and using the data needed to plan and monitor health sector interventions
- developing and implementing health-promoting and health-protecting policies and
- mobilizing and supporting other sectors.

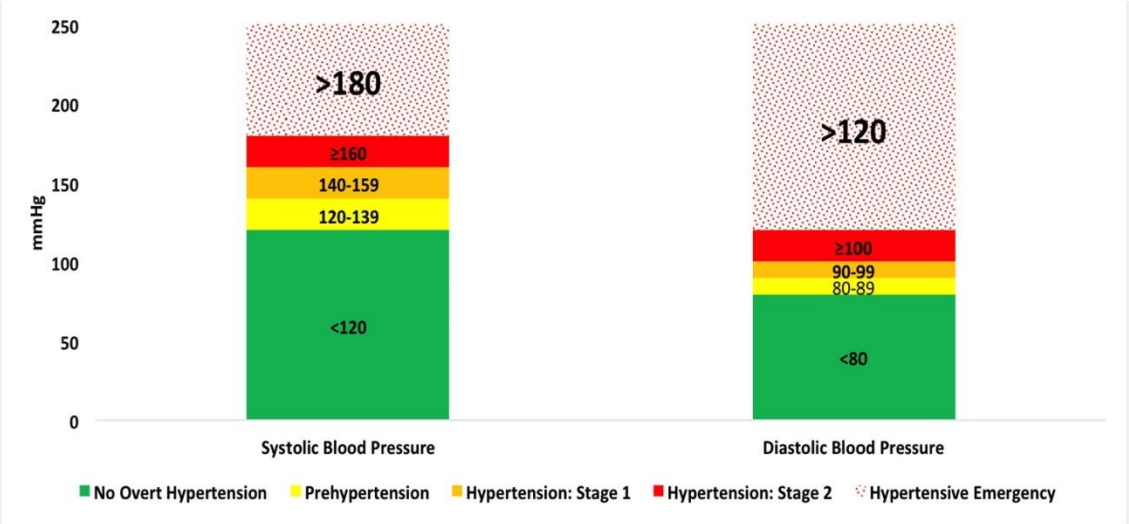
Actions aiming to improve adolescents' health not only has benefits to the adolescents now, but also has benefit to their future lives, even to their next generation. In the global perspective, improvements in adolescent health reduce present and future health costs and enhance social capital. It is required by WHO to put effort in urgent investment in adolescent health and well-being to achieve the 2030 Agenda for Sustainable Development (WHO, 2014a). This PhD project is relevant with the '*collecting and using the data needed to plan and monitor health sector interventions*', as it includes not only analysing existing data to study the association between diet and blood pressure levels in adolescents, but also developing new methods of monitoring blood pressure and carrying out health survey online in the United Kingdom (UK) adolescents.

1.1.2 Hypertension

Hypertension, also known as high or raised blood pressure, is a condition in which the blood vessels have persistently raised pressure. Each time the heart beats, it pumps blood into the vessels. Blood pressure (BP) is created by the force of blood pushing against the walls of blood vessels (arteries) as it is pumped by the heart (WHO, 2018c). The systolic blood pressure (SBP, higher number) is the force at which your heart pumps blood around your body. The diastolic blood pressure (DBP, lower number) is the resistance to the blood flow in the blood vessels. They're both measured in millimetres of mercury (mmHg). As a general guide: in adults, ideal blood pressure is considered to be between 90/60mmHg and 120/80mmHg, and high blood pressure is considered to be 140/90mmHg or higher, which means the systolic blood pressure is 140 mmHg or higher, and/or the diastolic blood pressure is 90 mmHg or higher (National High Blood Pressure Education, 2004) (

Figure 1.1). Hypertension can be caused by diseases such as renovascular disease, renal failure, pheochromocytoma or aldosteronism. When there is no demonstrable underlying cause of hypertension, the condition is called essential hypertension (primary or idiopathic hypertension). Essential hypertension is the most common type of hypertension, occurring in 95 percent of hypertension patients (Carretero and Oparil, 2000a).

Figure 1.1 Stages of Hypertension in adults (O'Shea et al., 2017)



There are several physiological mechanisms that involved in the development of hypertension:

Balance between cardiac output and peripheral resistance

The balance between the cardiac output and peripheral vascular resistance affects the level of blood pressure. In early stage of hypertension, the raised cardiac output is normally the main reason that causes blood pressure elevation. The raise peripheral resistance is then happened, which is related with the contraction of smooth muscle cells in walls of small arterioles, followed by the structural changes of the arteriolar vessel walls, such as thickening of the vessel walls and irreversible rise in peripheral resistance (Beevers et al., 2001).

Renin-angiotensin system

The renin-angiotensin system may be the most important of the endocrine systems that affect the control of blood pressure. Although the circulating renin-angiotensin system is not thought to be directly responsible for the rise in blood pressure in essential hypertension (Beevers et al., 2001, Berard et al., 2014), increasing evidence support that non-circulating “local” or “tissue” renin-angiotensin systems regulate blood pressure (Schulman et al., 2005, Hanna et al., 2002, Ackermann et al., 1998). The local generation of angiotensin II in the vasculature plays an important role in modulating the

balance between nitric oxide and reactive oxygen species (ROS) in the endothelium and thereby maintaining homeostasis of the vascular wall(Paul et al., 2006).

Autonomic nervous system

Sympathetic nervous system stimulation can cause both arteriolar constriction and arteriolar dilatation. It is also important in the mediation of short term changes in blood pressure in response to stress and physical exercise (Beevers et al., 2001).

Endothelial dysfunction

Endothelial dysfunction might be both a cause and consequence of high blood pressure. In experimental works, endothelial dysfunction caused by aging and the reduction of NO-dependent relaxation due to genetic, pharmacological or dietary (Wakui et al., 2013, Zhou et al., 2006, Korandji et al., 2011, Al-Awwadi et al., 2005) reasons was observed before the elevation of blood pressure, which is considered as the reason of hypertension. On the other hand, endothelial dysfunction observed in spontaneously hypertensive rats and borderline hypertensive rats was found as the consequence of hypertension, it happened after the elevation of blood pressure, and seemed to be associated with endothelium-derived constricting factors and not linked with NO levels (Bernatova et al., 2009, Mori et al., 2006, Gluais et al., 2005). However, it is very difficult to distinguish between primary and secondary endothelial dysfunction in experimental models of hypertension because the processes of endothelial function damage and elevation of blood pressure are many times occurring simultaneously.

Besides the abovementioned reasons, there are other mechanisms such as vasoactive substances, hypercoagulability, insulin sensitivity, genetic factors and intrauterine influences. The development of hypertension could be related to an interaction of all these factors.

Although the causes of essential hypertension are still not clear, a number of factors that were found to be related with increase blood pressure, for example obesity, insulin resistance, lack of exercises, aging, stress and dietary factors such as high alcohol intake, high salt intake and low potassium intake (Sever and Poulter, 1989, Carretero and Oparil, 2000b).

In 2008, approximately 40% of adults aged 25 and above had been diagnosed with hypertension all around the world; the number of people suffered from elevated blood

pressure rose from 600 million in 1980 to 1 billion in 2008(WHO, 2011). Hypertension is a leading risk factors for global mortality and a leading risk factor for cardiovascular disease (Angell et al., Moon et al., 2013). A large number of studies indicate that people with elevated blood pressure have a greater risk of having cardiovascular disease. For example, in the 1950s, the Framingham Heart Study had found that men/ women with hypertension (systolic blood pressure ≥160 mmHg and/or diastolic blood pressure ≥95 mmHg) had a 3-fold/6-folder greater rate of Coronary heart disease (CHD) events than those with normal blood pressure (systolic blood pressure <140 mmHg and diastolic blood pressure <90 mmHg) in the same age group (Franklin and Wong, 2013). In 2002, the Prospective Studies Collaboration (PSC) conducted a meta-analysis of prospective observational studies of the association between blood pressure and vascular mortality: irrespective of the baseline blood pressure, a 20 mmHg lower systolic blood pressure was found to be associated with a hazard ratio (HR) of 0.60 for ischemic heart disease (IHD) mortality (95% confidence interval (CI) 0.58–0.61) and a HR of 0.50 (95% CI 0.48–0.52) for stroke mortality in the age group with the largest number of fatal events (70–79 years)(Lewington et al., 2002). Other studies have supported this conclusion (Rutan et al., 1988, Rahimi et al., 2015, MacMahon et al., 1990, Rapsomaniki et al., 2014). As a risk factor of disease burden, hypertension has increased from the fourth ranked risk factor for global disease burden in 1990 to the leading risk factor in 2010, and the Global Burden of Disease Study 2010 (GBD 2010) suggested that high blood pressure caused 9.4 (95% CI, 8.6-10.1) million deaths, 162 million years of life lost and 173 million disability-adjusted life years per year, accounting for 17.8% of premature death and 7.0% (95% CI, 6.2%–7.7%,) of DALYs lost globally(Lim et al., 2012, Campbell et al., 2015).

1.1.3 Hypertension in adolescents

Although cardiovascular disease is not a leading cause of death or cause of lost DALY in adolescents, and the burden of elevated blood pressure is concentrated in older populations (Rahimi et al., 2015), recently epidemiology studies revealed that elevated blood pressure is becoming a problem that should be taken into consideration among adolescents. According to the results of United States National Health and Nutrition Examination Survey (NHANES), the prevalence of hypertension in children and adolescents is increasing. In children aged 8 to 17, after age, ethnicity, and sex standardization, SBP was 1.4 (95% CI, 0.6-2.2) mmHg higher and DBP was 3.3 (95% CI, 2.1-4.5) mmHg higher in 1999-2000 compared with 1988-1994. At the same time,

slightly more than 1 in 10 of this population had either borderline high (SBP and/or DBP at the 90th percentile or higher but < 95th percentile, or as BP levels of 120/80mmHg or higher but <95th percentile) or high blood pressure (SBP and/or DBP at the 95th percentile or higher) (Kit et al., 2015, Muntner et al., 2004).

Moreover, elevated blood pressure in youth is a strong predictor of hypertension in adulthood (Lauer and Clarke, 1989, Bao et al., 1995, Tirosh et al., 2010). A study reported that blood pressure trajectories that begin as early as 7 years of age and then track into adulthood, indicating that children and adolescents with elevated blood pressure were more likely to develop into hypertensive adults (Theodore et al., 2015). A meta-regression analysis of 50 cohort studies in diverse populations reported that blood pressure in early life stage is strongly correlated with blood pressure in adulthood (Chen and Wang, 2008). The Fels Longitudinal Study has founded that even a single elevated blood pressure reading during childhood increases the risk of adulthood hypertension and metabolic syndrome, with the risk increasing as the number of elevated readings during childhood increases (Sun et al., 2007). Even in those adolescents with normotensive levels of blood pressure, a higher blood pressure predicts hypertension in young adulthood (Tirosh et al., 2010). Target organ damage also started to appear in children with elevated blood pressure such as left ventricular hypertrophy (Brady et al., 2010, Kollias et al., 2014) and retinopathy (Conkar et al., 2015). It is concluded that the progression of development of hypertension started at early age of life, and will track into adulthood if there if no intervention given to control the blood pressure of children and adolescent. It is a reasonable assumption that the current increased prevalence of paediatric hypertension could lead to a relevant high burden of adulthood hypertension in the following decades.

Therefore, it is highly important to carry out effective preventive interventions among adolescents to help them reduce blood pressure or maintain normal blood pressure, for example conducting hypertension screening and carrying out intervention on diet or life habits. In the year of 2017, American Academy of Pediatrics (AAP) recommended in *the 2017 AAP Clinical Practice Guideline on Blood Pressure Management in Children* that blood pressure should be measured annually in children and adolescents $\geqslant$ 3 years of age (Dionne, 2017). Lifestyle modification, including dietary changes and increased physical activity were also recommended to control blood pressure in children and adolescents (Samuels and Samuel, 2018).

1.1.4 Factors affecting blood pressure in adolescents

To determine risk factors of elevated blood pressure is a prerequisite for prevention. According to Guidelines for Management of Hypertension published by the British Hypertension Society in 2004 (Williams et al., 2004), many risk factors had been reported to elevate blood pressure in adults, like obesity, lack of physical activities, cigarette smoking, alcohol intake, highly intake of salt and fat. Other factors like family history (Muldoon et al., 1993), social economic status (Colhoun et al., 1998, Krieger et al., 2014) and ethnicity (Gasevic et al., 2015, Piper et al., 2014, Krieger et al., 2014) had also been proved to affect blood pressure.

In adolescents, some same factors were found to affect blood pressure, including obesity (Wong et al., 2013, Kelishadi et al., 2013, Sugiyama et al., 2007), smoking (Huntington-Moskos et al., 2014, Hacke and Weisser, 2015, Giussani et al., 2013), alcohol intake (Zhang et al., 2013, Riley and Bluhm, 2012), lack of physical activities (So et al., 2013, Yoshinaga et al., 2011, Sugiyama et al., 2007, Pahkala et al., 2012, Dennison, 2012), family history (Xu et al., 2015, Westerdahl et al., 2013), social economic status (Kaczmarek et al., 2015, Griffiths et al., 2012), ethnicity (Noor et al., 2013, Fang et al., 2012, Hemmings et al., 2011a, Hemmings et al., 2011b, Harding et al., 2006) and dietary factors, etc. For example, adolescents of different ethnicities might have different levels of risk to have hypertension. SBP of British South Asian adolescents was 6.9 mmHg (95% CI: -13.4 mmHg to 0.4 mmHg) higher than their British white counterparts (Hemmings et al., 2011b), DBP of Indian girls was1.2 mmHg (95% CI: 0.1mmHg to 2.4 mmHg) higher than white girls (Harding et al., 2006). However, study also reported that white adolescents might have higher blood pressure than black Caribbean black African, Indians, Pakistanis, Bangladeshis and mixed ethnicity adolescents (Harding et al., 2006). Among these risk factors for elevated blood pressure, dietary factors are suggested to be among the most important ones.

Different from adults, where essential hypertension is the most common type of hypertension (Carretero and Oparil, 2000a), most hypertensive children and adolescents have underlying cardiorenal disease resulting in secondary hypertension. In children and adolescents who have essential hypertension, obesity is the most common reason. In United States, in the year of 2001 to 2016, nearly half of the net increase in new

diagnoses of hypertension among youths would be among those with obesity (Jackson et al., 2018).

1.1.5 Online epidemiology research in adolescents

In many disciplines, carrying out research online rather than using traditional face-to-face methods is becoming more and more popular in the recent decades (Wright, 2004, Wright, 2005), including in the area of medicine (Fenner et al., 2012, Gunasekaran et al., 2013). With the development of Internet technologies, recruiting participants, completing questionnaire and recording diet can all be done online. Online research allows researchers to obtain a sample from a wider geographical area, with lower costs in terms of time and/or money (Batterham, 2014). At the same time, carrying out research online is more convenient to the participants and more acceptable for them when collecting sensitive information and/or with vulnerable populations (Cantrell and Lupinacci, 2007). However, it is seldomly used in exploring the association between diet and blood pressure, especially in adolescents.

In the recent years, adolescents who use Internet had been growing exponentially (Gross, 2004). According to the Graphics, Visualization, and Usability Center at the Georgia Institute of Technology, 32% of 11-to-20- year-olds spend 10 to 20 hours a week online in 1998 (Montgomery, 2001). The Orgnization for Economic Co-operation and Development (OECD) reported that in the year of 2015, in OECD countries, almost every 15 years old student had access to the Internet at home, and 91% of them had a smart phone that connected to the Internet. The adolescents spent 2.5 to 3 hours per day online (OECD, 2017). In the UK, a third of 15 year olds are ‘extreme internet users’, defined as who uses the internet for more than six hours outside of school on a typical weekend day. The young people are heavier users of social networking websites (Gu et al., 2016, Madden et al., 2013). In 2012 to 2013, 11% of UK 10 to 15 year old girl s and 5 % of boys spent over three hours on social networking websites on a normal school day (2015b), while in the year of 2015, 95% of the 15 year old UK adolescents used social networking websites before or after school (Firth, 2017). On the other hand, advertising on Internet target on children and adolescents has becoming more and more popular (Strasburger and Donnerstein, 1999, Communications et al., 2006). Thus situation indicates that recruiting adolescent participants online, especially through social media websites, such as Facebook and Instagram, is possible and could be effective.

Recruiting participants online through social media websites had been explored by some researchers in both adults and adolescents, in the area of psychology and medicine (Fenner et al., 2012, Gunasekaran et al., 2013, Miyagi et al., 2014, Thornton et al., 2016, Chu and Snider, 2013, Cowie and Gurney, 2018, Whitaker et al., 2017, Adam et al., 2016). The strength of online recruitment that had been mentioned in several studies is that it had been proved to be effective and cost-efficient by some of the studies (Christofides et al., 2009, Raacke and Bonds-Raacke, 2008, Ramo and Prochaska, 2012, Fenner et al., 2012, Frandsen et al., 2016). Fenner carried out an exploratory study in Australia by placing advertisement on Facebook, recruiting 16 to 25 years old female participants for a health study. A total of 551 females responded to the advertisement, of home 278 completed the survey in a period of four months. The cost for each compliant participant was US $20, making this highly cost effective (Fenner et al., 2012). On the other side, the weakness of online recruitment that should be considered is that the demographic information of the participants recruited through Internet may be different from those recruited in traditional methods. Frandsen found participants recruited online was younger and less confident in quit smoking (Frandsen et al., 2016). The study involves dietary assessment and blood pressure measurements will be more complicated than the studies mentioned above. It is anticipated that the response rates in dietary study could be lower. Therefore, a pilot study is needed to explore the feasibility to do online recruitment and online research in the area of diet and blood pressure.

Several websites (for example, Bristol Online Survey and Qualtrics) are available to conduct online questionnaire surveys. With templates of different kinds of questions provided by the websites, the questionnaire could be easily transformed to an online form. It is convenient for the participants to compete the questionnaire whenever and wherever they like, using personal computer (PC), lab top or even mobile phones. Consent can also be obtained online using this method. Data on these websites is safe-guarded. The websites provide a unique username and password to the researcher, to make sure data can only be accessed by authorised people. At the same time, all the data is encrypted,access to sensitive data is strictly limited to technical teams of the website.

Online diet record is a novel area in nutritional epidemiology. Myfood24 is a website designed to collect diet data online (Carter et al., 2016, Cade, 2017). Participants can access the website through a link provided by the researcher. Detailed and easy to follow instruction on how to record diet on the website is given to the participants before they start recording their diet. Common brands of food in the UK are included in

the database, and pictures of portion sizes are displayed on the website, which will make the participants record their diet more accurately. This online diet record tool is validated in UK adolescents (11 to 18 years) and adults (19 – 64 years) (Carter et al., 2015, Albar et al., 2016).

In conclusion, carrying out survey to explore the association between diet and blood pressure in adolescents is necessary, and the feasibility of conducting online survey in that area need to be tested.

1.2 Aims

1.2.1 Overall Aims of the PhD project:

The aim of the study it to develop a pilot online research method to explore the association between diet and blood pressure in adolescents. There are two main objectives:

a) to find out key dietary factors that may affect blood pressure levels in adolescents using existing data, and

b) to explore the feasibility of use new technology (for example online recruitment, online questionnaire, online dietary record, blood pressure measurements, etc.) in epidemiology studies.

1.2.2 Objectives of each chapter (Figure 1.2):

Chapter 1: To build up an overall view of studies published on dietary factors and blood pressure in adolescents through literature review, and then determine the main dietary factors to take into consideration in the PhD program.

Chapter 2: To determine the cross-sectional relationships between dietary factors and blood pressure levels in UK adolescents aged 10-19 years, according to National Dietary and Nutrition Survey (NDNS) 2008-2014, and to find out important dietary factors that may affect blood pressure as exposures in the following analyse.

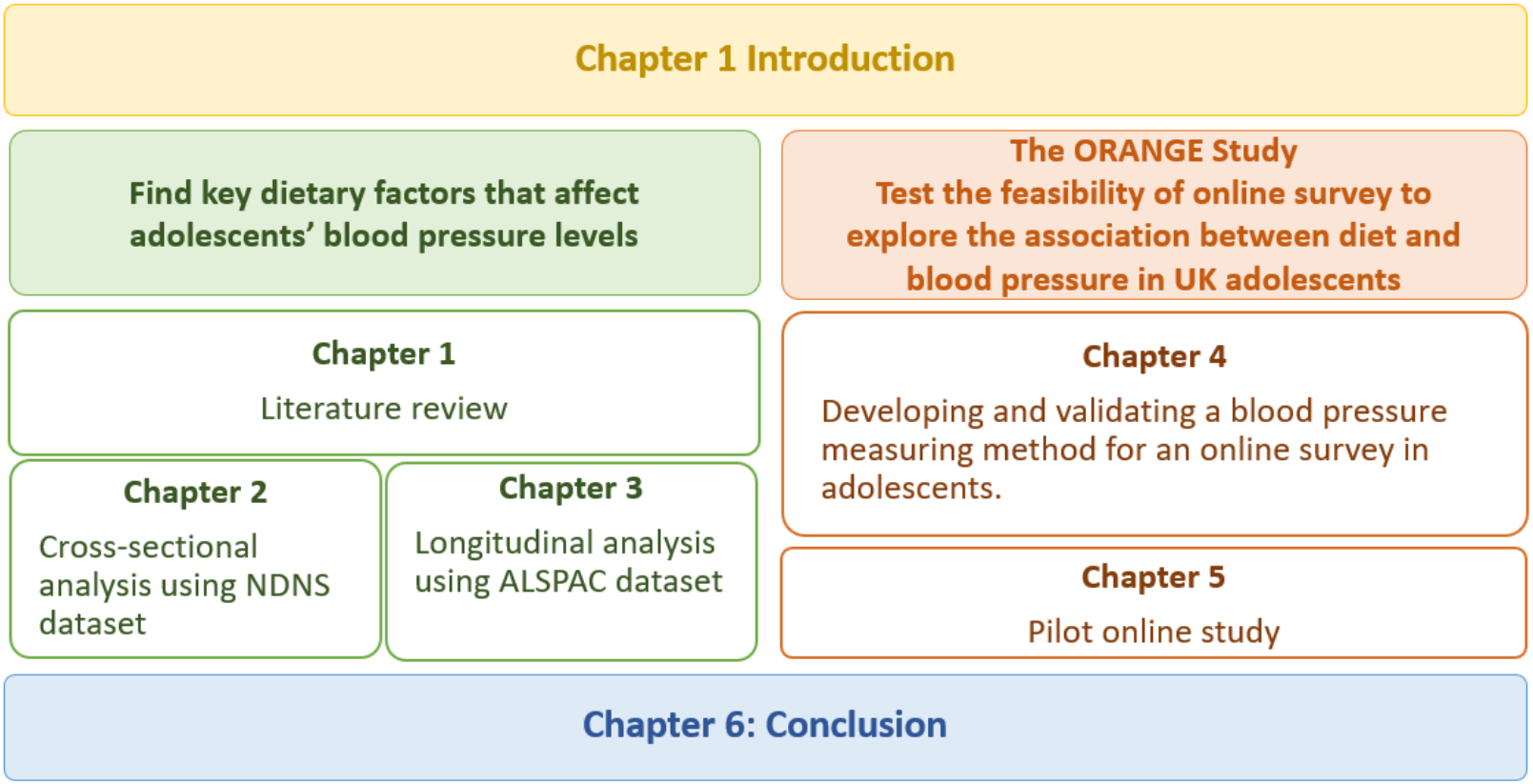
Chapter 3: to determine the longitudinal relationships between 1) dietary vitamin E intake and later blood pressure levels and 2) dietary fats intake and later blood pressure levels in UK adolescents using Avon Longitudinal Study of Parents and Children (ALSPAC) dataset.

Chapter 4: To explore the accuracy of using smart phone applications to measure blood pressure values, to validate the accuracy of self-measured blood pressure values in

adolescents, and then develop an appropriate method of blood pressure measurement to be used in an online health survey

Chapter 5: Chapter 5 has two parts. The objectives of Part A (survey of adolescents' attitudes on an online health research) are to investigate adolescents' attitudes on online health survey by face-to-face questionnaire, and design the protocol of pilot survey (Part B) based on the results. The objectives of Part B (pilot online survey) is to test the feasibility, explore the advantages and disadvantages of online research by carrying out a pilot online survey.

Figure 1.2 Structure of PhD project



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1.3 Literature review on diet and blood pressure in adolescents

1.3.1 Aim of the literature review

The aim of this literature review is to draw an overview of the studies in the area of diet and blood pressure in adolescents, and find gaps to fill in this area. As studies published before the year of 2011 had been reviewed and summarized (Simons-Morton and Obarzanek, 1997, Arts et al., 2014), and considering the tim limitation of the whole PhD programme, the screened period was restricted to the recent four years. This literature review is a "scoping review" rather than a "systematic review". A scoping review is a process of mapping the existing literature or evidence base. The difference between systematic review and scoping review can be found in Table 1.1 (Armstrong et al., 2011, Brien et al., 2010)

Table 1.1 Comparison between systematic and scoping reviews

(Armstrong et al., 2011, Brien et al., 2010)

Systematic review	Scoping review
Focused research question with narrow parameters	Research question(s) often broad
Inclusion/exclusion usually defined at outset	Inclusion/exclusion can be developed *post hoc*
Quality filters often applied	Quality not an initial priority
Detailed data extraction	May or may not involve data extraction
Quantitative synthesis often performed	Synthesis more qualitative and typically not quantitative
Formally assess the quality of studies and generates a conclusion relating to the focused research question	Used to identify parameters and gaps in a body of literature

1.3.2 Searching strategy

The first searching was done between October 2014 and July 2015, with the public date restricted to from 01/01/2011 to 31/05/2015. A second searching was done in November and December 2017 to update the new studies, the public date was restricted to 01/06/2015 and 31/10/2017. In these two searches, papers were found in Pubmed, Ovid Medline (1996 to current) and Global Health (1973 to current) using the following combination of terms in all fields:

diet* AND ((blood pressure) OR hypertens*) AND adolescen*

Relevant references of the selected papers were also included into the dataset. The exclusion criteria is:

a) Reviews
b) Studies where all the participants were adults over 20 years old or children under 10 years old.
c) Studies where the participants were patients of diabetes, kidney diseases or other disease, but studies where participants had hypertension or prehypertension were not excluded.
d) Studies where the exposure factors did not include any dietary factor.
e) Studies where the outcome factors did not include blood pressure values or prevalence of hypertension, such as studies used total prevalence of cardiovascular disease, cardiovascular disease risk or prevalence of metabolic syndrome as outcome. Those studies use metabolic syndrome as outcome, but meanwhile analyzed each components (which means blood pressure data was analyzed as an independent outcome) were included.

After reading the abstracts of each paper, papers were excluded if they met one or more of the exclusion criteria.

The following contents were extracted from each included paper:

- Title of the paper
- First author
- Year of publication
- Research name (if available)
- Study design
- Sample size
- Characteristic of participants (age, gender, ethnicity, healthy or not)
- Dietary assessment method
- Statistics methods (type of analysis used, factors adjusted as confounders in the models)
- Main result (positive/negative relationship, parameters to estimate the relationship, confidential intervals and p values)

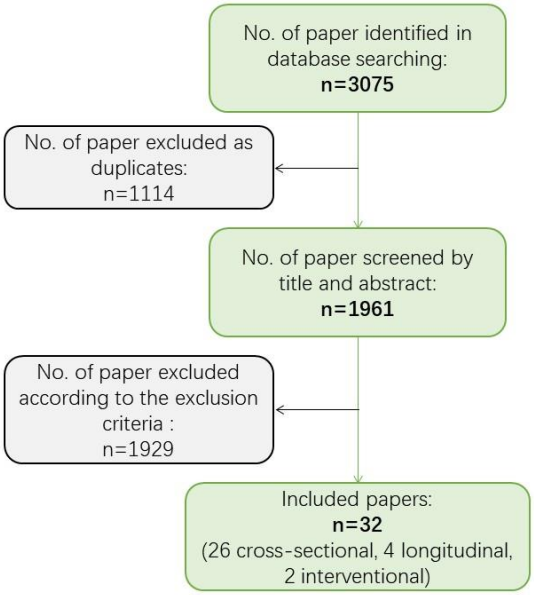
The findings from previous studies were collected and analysed , according to the dietary factors that they studied. For each dietary factor, the number of related studies, the above information of every study were summarized.

1.4 Results

1.4.1 General information

3075 papers were identified that met the inclusion criteria. From them 3043 papers were excluded according to the exclusion criteria, and 32 papers remained which reported results of individual studies that had measured diet and BP in adolescents (inclusion and exclusion of publications at each stage of the literature review can be found in Figure 1.3). A summary of first author, study design, sample size, dietary assessment method and included dietary factors and results are listed in Table 1.2 and Table 1.3.

Figure 1.3 Literature review flow chart



In all the studies, 30 were observational studies (26 were cross-sectional and 4 were longitudinal observational studies), and 2 were interventional studies. In the 30 observational studies, 13 used Food Frequency Questionnaire (FFQ) to assess dietary information, 6 used dietary recall or diet history method, 6 used dietary records, 5 used questionnaires and 1 used 24-h urine tests to indicate sodium and potassium intake.

Table 1.2 Summary of methods of the included papers

Author and year of publish	Study design	Sample size	Sample characters	Dietary assessment method
(Ambrosini et al., 2013a)	cross-sectional	1433	14-17 years	FFQ
(Aounallah-Skhiri et al., 2011)	cross-sectional	1019	15-19 years	FFQ
(Asghari et al., 2016)	cross-sectional	424	6-18 years	FFQ
(Bobridge et al., 2013)	cross-sectional	814	13-15 years	dietary record
(Buendia et al., 2015)	longitudinal, 10 years of follow up	2185	9 to 10 years at baseline, girls	dietary record
(Campanozzi et al., 2015)	cross-sectional	1424	6-18 years	24-hour urine test
(Chan et al., 2014)	cross-sectional	2727	12-16 years, Chinese	FFQ
(Chmielewski and Carmody, 2017)	cross-sectional	4716	12-14 years	interview
(DellaValle et al., 2017)	cross-sectional	117	4-17 years	FFQ
(de Moraes et al., 2015)	cross-sectional	1605	12.5-17.5 years	24-hour dietary recall
(Gilardini et al., 2015)	cross-sectional	448	6-18 years, obese	7-day diet history
(Gopinath et al., 2012)	longitudinal, 5 years of follow up	858	12 years at baseline	FFQ
(Heidari-Beni et al., 2015)	cross-sectional	205	11-13 years, girls only	FFQ
(Jayashri et al., 2015)	cross-sectional	495	10-19 years, Indian	questionnaire
(Kajale et al., 2016)	cross-sectional	417	10-14 years, Indian	3-day 24-hour dietary recall

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(Kim et al., 2017)	cross-sectional	136739	9, 12 and 15 years, Korean	FFQ
(Loh et al., 2017)	cross-sectional	873	13 year, Malaysian	questionnaire
(Machado et al., 2015)	interventional, 11 weeks	75	13.7 ± 2.1 years, obese	/
(McCourt et al., 2014)	cross-sectional	487	12-15 years	7-day diet history
(Mirza et al., 2013)	interventional, 2 years	113	7-15 years, obese	/
(Mu et al., 2014)	cross-sectional	1319	16-18 years, Chinese	FFQ
(O'Neil et al., 2012)	cross-sectional	5811	12-18 years	dietary recall
(Payab et al., 2016)	cross-sectional	13486	6-18 years	FFQ
(Ponzo et al., 2015)	cross-sectional	1200	11-13 years	FFQ
(Prasad et al., 2017)	cross-sectional	1041	15.1 ± 1.4 years, Indian	oral questionnaire
(Setayeshgar et al., 2017b)	longitudinal, 2 years of follow up	448	10-17 years at baseline	dietary record
(Shi et al., 2014)	longitudinal, 14 years of follow up	435	The median age was 6 years at baseline and 16 years during the last assessment	dietary record
(Smith and Franzen-Castle, 2012)	cross-sectional	335	Mmong	24-h dietary recall
(Souza et al., 2016)	cross-sectional	488	Mean age was 11 years	FFQ
(Woodruff et al., 2014)	cross-sectional	1068	10-14 years	food behaviour questionnaire
(Yoshinaga et al., 2011)	cross-sectional	755	15-18 years	FFQ
(Zhu et al., 2014)	cross-sectional	672	15-18 years, Chinese	dietary record

FFQ: Food Frequency Questionnaire

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Table 1.3 Summary of results of the included papers

Author and year of publish	Studied dietary factors	Summary of results	Notes
(Ambrosini et al., 2013a)	SSB	Increases in SBP were linked with increasing SSB intakes	The Western Australian Pregnancy Cohort (Raine) Study
(Aounallah-Skhiri et al., 2011)	energy, dietary pattern	An increase in levels of high blood pressure with tertiles energy intake. A modern dietary pattern was associated with decreased prevalence of hypertension.	
(Asghari et al., 2016)	salty snacks	The risk of incident hypertension is higher in the participants that had higher salty snacks intake	
(Bobridge et al., 2013)	carbohydrate	No significant relationship between diet fructose intake and blood pressure was found, but fructose intake was related with serum uric acid	the Western Australian Pregnancy Cohort (Raine) Study

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(Buendia et al., 2015)	sodium, potassium	No significant association was found between sodium intake and blood pressure. Potassium intake was linked with lower SBP and DBP. Negative association between potassium to sodium ratio and systolic blood pressure was found.	
(Campanozzi et al., 2015)	sodium	Higher 24-h urinary sodium excretion and potassium excretion were both linked with higher SBPZ	
(Chan et al., 2014)	SSB	An increased SSB intake was linked to higher SBP	
(Chmielewski and Carmody, 2017)	sodium, potassium	Negative association between potassium to sodium ratio and systolic blood pressure.	National Health and Nutrition Examination Survey
(DellaValle et al., 2017)	dairy	Negative association between dairy intake and SBP	
(de Moraes et al., 2015)	protein	Negative association between protein intake and DBP	
(Gilardini et al., 2015)	protein	Negative association between vegetable protein intake and BP	

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(Gopinath et al., 2012)	carbohydrate, fibre	Higher glycemic index, glycemic load, total sugar and fructose were all associated with higher DBP. Higher dietary fibre was associated with lower BP	
(Heidari-Beni et al., 2015)	FVI	Potato consumption was not linked with BP	
(Jayashri et al., 2015)	salt	Additional salt intake and papad/pickle intake was linked with prevalence of hypertension	
(Kajale et al., 2016)	calcium	Low dietary calcium intakes was linked with higher risk of hypertension	
(Kim et al., 2017)	FVI, meat, dairy	Higher level of meat consumption was associated with lower BP. The intake of milk, fruit, and vegetables was not associated with BP.	Korea School Health Examination Survey (KSHES)
(Loh et al., 2017)	SSB	U-shaped association was found between SSB intake and BP	
(Machado et al., 2015)	flaxseed	Participants who received brown and golden flaxseed had lower DBP at the end of the study	

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(McCourt et al., 2014)	dietary pattern	Sweet tooth dietary pattern was linked with higher BP	the Northern Ireland Young Hearts Project
(Mirza et al., 2013)	carbohydrate, fat	BP lowered in group received combined of low-fat diet and low-glycemic load diet	
(Mu et al., 2014)	dietary pattern	Animal protein pattern was linked with higher risk of hypertension	
(O'Neil et al., 2012)	nuts	No relationship was found between nuts intake and BP	
(Payab et al., 2016)	FVI	No relationship was found between FVI intake and BP	
(Ponzo et al., 2015)	salt	Higher salt intake from snacks was associated with higher BP	
(Prasad et al., 2017)	FVI	Low fruit diet was linked with higher risk of hypertension. No relationship was found for vegetable intake.	
(Setayeshgar et al., 2017b)	fat, sodium, FVI	Dietary fat at baseline was associated with increases in BP, higher sodium intake at baseline was associated with an increase in DBPZ, VFI was not associated with change in BP	
(Shi et al., 2014)	salt, FVI	Higher salt intake was associated with increased SBP, lower FVI was associated with higher BP	

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(Smith and Franzen-Castle, 2012)	carbohydrate, protein, fat, Ca, dairy	Energy, protein, total fat intake was not linked with BP. Negative relationship between total carbohydrate intake and BP was found. Calcium intake was associated with lower SBP but higher DBP. Higher dairy intake was associated with decreased DBP.	
(Souza et al., 2016)	SSB	Diet soft drink consumer had higher BP	
(Woodruff et al., 2014)	salt	No association between salt intake and blood pressure	No confounder adjusted in the analysis
(Yoshinaga et al., 2011)	energy, fibre	Total energy intake was found to be linked with higher SBP. No relationship was found between fiber intake and BP.	The Amsterdam Growth and Health Study
(Zhu et al., 2014)	carbohydrate	High carbohydrate intake was associated with lower SBP	

SSB: sugar-sweetened beverages FVI: fruit and vegetable intake

BP: blood pressure SBP: systolic blood pressure SBPZ: systolic blood pressure z-score DBP: diastolic blood pressure

DBPZ: diastolic blood pressure z-score

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1.4.3 Association between blood pressure and dietary energy intake

Three observational studies were found (Yoshinaga et al., 2011, Aounallah-Skhiri et al., 2011, Smith and Franzen-Castle, 2012), and all of them were cross-sectional, where participants' age ranged from 9-19. Two of them (Yoshinaga et al., 2011, Aounallah-Skhiri et al., 2011) used food frequency questionnaire, and the other (Smith and Franzen-Castle, 2012) used 24-h dietary recall to collect dietary data. Two of them found positive relationships between total energy intake and blood pressure (Yoshinaga et al., 2011, Aounallah-Skhiri et al., 2011), the other found no relationship (Smith and Franzen-Castle, 2012).

Yoshinaga built a model adjusted for exercise time, TV-watching time, regular breakfast, fiber/1000 Kcal, parental BMI, paternal exercise time, maternal BMI, maternal exercise time in male adolescents to predict systolic blood pressure (Yoshinaga et al., 2011), and found total energy intake was associated with higher systolic blood pressure, but such relationship was not found in girls. In the other cross-sectional study (Aounallah-Skhiri et al., 2011), after adjustment for physiological factors and physical activity, an increase trend of blood pressure was found in different tertiles of total energy intake in girls but not in boys. In both of these two studies, the researchers adjusted for some factors, but some of the essential potential confounders such as smoking, alcohol, intake of other nutrients were not adjusted; also the method used to collect diet data was FFQ, therefore, the energy intake calculation might be not as accurate as where dietary recall or dietary record were used. Smith used diet recall to collect dietary data, and found no relationship between dietary total fat intake and blood pressure (Smith and Franzen-Castle, 2012). However this result could be biased as for in the regression analysis in this study, age, anthropometric variable (including BMI; triceps, biceps, subscapular and suprailiac skinfolder; arm, hip and waist circumference; waist-height-ratio) and dietary variables (including energy, protein, carbohydrate, fat, calcium, magnesium, potassium and sodium) were all put into the model. However, this approach may lead to over-adjustment because the confounders may interact with each other, for example BMI and energy intake, BMI and the other anthropometric variables. On the other hand, the other potential confounders such as smoking, physical activities were not adjusted.

1.4.4 Association between blood pressure and dietary nutrients

Macronutrients

Carbohydrate

Five studies were found, of which 2 studies are cross-sectional (Zhu et al., 2014, Smith and Franzen-Castle, 2012) and reported result about total dietary carbohydrate intake, 1 study is cross-sectional study about dietary fructose (Bobridge et al., 2013), 1 study is longitudinal study about dietary glycemic index and glycemic load (Gopinath et al., 2012), and the other is interventional study about dietary glycemic load (Mirza et al., 2013).

For the 2 cross-sectional studies (Zhu et al., 2014, Smith and Franzen-Castle, 2012) focussed on total carbohydrate intake, their sample sizes are 335 and 672, and participant's age ranged from 9 to 18 years old. One of them used 3-day diet diary, and the other used 24-hour diet recall to collect diet data. Both of them found a negative relationship between total carbohydrate intake and blood pressure only in males. The other cross-sectional study used 3-day diet diary to collect fructose intake data among 814 thirteen to fifteen years old adolescents (Bobridge et al., 2013). No significant relationship between diet fructose intake and blood pressure was found, but fructose intake was related with serum uric acid, which was reported to positively related with systolic blood pressure.

Two studies reported positive relationship between glycemic index/glycemic load and blood pressure. A longitudinal study (Gopinath et al., 2012) used 120-item self-administered FFQ to collect diet data among 858 adolescents. The result shows that among girls, each 1 SD increase in dietary glycemic index was concurrently related to increase of systolic blood pressure by 1.81 mmHg, while glycemic load was concurrently related to increases of systolic blood pressure and diastolic blood pressure by 4.02 mmHg and 2.63 mmHg separately, and no relationship was found among boys. A two-year randomized controlled trial (Mirza et al., 2013) in 113 seven to fifteen years old Hispanic obese children found both systolic and diastolic blood pressure were decreased in a combined group of those received low-fat and low-glycemic-load diet.

Fat

The mechanism of how fat affects blood pressure level can be found in Chapter 2.

One cross-sectional observational study (Smith and Franzen-Castle, 2012), one longitudinal (Setayeshgar et al., 2017a) observational study and one randomized controlled trial (Mirza et al., 2013) were found. In these three studies, participants' age ranged from 7 to 19, and sample size ranged from 113 to 448.

The cross-sectional study (Smith and Franzen-Castle, 2012) used diet recall to collect dietary data, no relationship between dietary total fat intake and blood pressure was found. The results could be biased for not appropriately including confounders in the regression model, a detailed explanation of this can be found in section 4.1.2. In the longitudinal study (Setayeshgar et al., 2017a), Setayeshgar found fat intake at baseline (participants aged 10 to 17) was associated with increased SBPZ and DBPZ two years later. Dietary record was used in this study.

A two-year randomized controlled trial (Mirza et al., 2013) in 113 seven to fifteen years old Hispanic obese children found both systolic and diastolic blood pressure were decreased in a combined group of those received low-fat and low-glycemic-load diet. However the independent effect of each factor was not determined.

Protein

Three cross-sectional studies were identified (de Moraes et al., 2015, Gilardini et al., 2015, Smith and Franzen-Castle, 2012). The participants' age ranged from 6 to 18 years old, and the sample size ranged from 335 to 1605. Two of them used 24-hour diet recall and the other used 7-day diet history method to collect diet data. Two studies found negative association between protein intake and blood pressure (de Moraes et al., 2015, Gilardini et al., 2015), one found no association (Smith and Franzen-Castle, 2012).

De Moraeset (de Moraes et al., 2015) studied dietary protein, amino acids intake and blood pressure in 12.5 to 17.5 years old adolescents. A negative association between protein intake and DBP was found in males, but no association was found in females. Positive association between histidine and SBP was found in both males and females, positive association between methionine and DBP, negative associations between tyrosine and both SBP and DBP were found in females. Blood pressure was transformed to blood pressure Z-score according to age, gender and height. Gilardini (Gilardini et al., 2015) studied the relationships between dietary habits and cardiometabolic health among Italian obese children and adolescents aged 6 to 18 years.

After adjusting for age, gender and waist-height-ratio, vegetable protein intake was linked with lower systolic blood pressure. Smith found no association between protein intake and blood pressure in 9 to 18 years olds (Smith and Franzen-Castle, 2012).

Dietary Fibre

The potential antihypertensive mechanisms of dietary fiber could be: a) Prevention on insulin resistance. Insulin resistance is implicated in the development of hypertension, and dietary fibers may affect blood pressure by modulating insulin metabolism (Ferri et al., 1999, Zhang et al., 2012a). b) Reduction in serum cholesterol level. Lower plasma cholesterol concentrate was associated with improved endothelium vasodilation, which is associated with reduced blood pressure (Anderson et al., 1995, Vogel et al., 1996). c) Weight loss. Lower body weight was suggested as a potential mechanism to decrease high blood pressure levels (Neter et al., 2003, Howarth et al., 2001, Slavin, 2005).

Two observational studies were found, one was cross-sectional study (Yoshinaga et al., 2011), and the other a longitudinal study (Gopinath et al., 2012).

In the cross-sectional study, participants' age range from 15 to 18 years old, and the sample size was 755. No relationship between dietary fibre intake and blood pressure was found after adjusted for exercise time, Television-watching time, regular breakfast, parental Body Mass Index (BMI), paternal exercise time, maternal BMI, maternal exercise time.

The longitudinal study (Gopinath et al., 2012) was a 5 years study, baseline age of participants is 12, sample size is 858. In females, after adjusting for age, ethnicity, parental education, parental history of hypertension, baseline height, baseline blood pressure, change in body mass index, and time spent in physical and sedentary activities, each 7.1g/d dietary fibre intake at baseline was related with a 0.96 mmHg, 0.62 mmHg, and 0.75 mmHg decrease in systolic blood pressure, diastolic blood pressure, and arterial blood pressures respectively after 5 years from baseline, but these results were not found in boys.

In conclusion, these two studies all have sufficient sample size and had adjusted for most potential confounders. Conflicting results were reported, therefore, further study on the relationship between dietary fibre intake and adolescents' blood pressure should be undertaken.

Mineral

Magnesium

The potential mechanisms by which magnesium lowers BP are: a) Acting like a natural calcium channel blocker. Magnesium competes with sodium for binding sites on vascular smooth muscle cells, induces endothelial-dependent vasodilation, improves endothelial dysfunction, decreases intracellular calcium and sodium and reduces BP (Barbagallo et al., 2010, McCarty, 1996). b) Acting as an essential cofactor for the delta-6-desaturase enzyme. The delta-6-desaturase enzyme increases the conversion from linoleic acid to prostaglandin E1, which is a vasodilator and a platelet inhibitor (Das, 2010, Das, 1989, Das, 2006). c) Regulating intracellular calcium, sodium, potassium, insulin sensitivity and arterial compliance (Resnick, 1997, Hatzistavri et al., 2009).

One cross-sectional study (Smith and Franzen-Castle, 2012) was identified. Participants' age ranged from 9 to 18 years, 24-h dietary recall was used to assess diet. No significant association between dietary magnesium and blood pressure was found. The potential bias in the regression analysis was explained in section 1.4.2.

Calcium

There are several potential mechanisms that can explain how calcium regulates blood pressure levels: a) Higher intake of calcium is linked with decreasing calcium influx in vascular smooth muscle cells (Zemel, 2001), reducing intracellular calcium levels and reducing vascular smooth muscle cells contractions (Bohr, 1963). b) Increasing adipocyte lipolysis and decreasing lipogenesis (Zemel, 1998, Zemel, 2002). c) decreasing plasma renin activity (Touyz et al., 1995). d) Regulating energy metabolism and reducing weight gain (Zhang et al., 2012b, Van Loan, 2009). e) reducing insulin resistance (dos Santos et al., 2008, Ma et al., 2006).

Two observational studies were found, both of them are cross-sectional, one had participants age ranged from 10 to 14, sample size 417 (Kajale et al., 2016), and the other had participants age ranged from 9 to 18, sample size 335 (Smith and Franzen-Castle, 2012). Both of them used diet recall to collect dietary data. Conflicting results were reported in these two studies.

In one study, 417 healthy adolescents were studied. Calcium intake was linked with lower blood pressure ($r=-0.120$, $p<0.010$) after adjusted for energy intake, but the author

did not indicate the outcome is SBP or DBP. In the other study (Smith and Franzen-Castle, 2012) by Smith, calcium intake was associated with lower systolic blood pressure but higher diastolic blood pressure in girls. No relationship was found in boys. For these two studies, not adjusting for confounders such as smoking, alcohol intake or energy intake might cause bias in the results, and the other potential bias in Smith.'s study had been explained in section 1.4.2.

Potassium and sodium

The mechanisms of the antihypertensive effect of potassium are: a) increased serum potassium is associated with stimulation of Na+-K+ ATPase pumps, increases in the number of Na+-K+ ATPase pumps in basolateral cell membranes, increases in the transepithelial voltage, the opening of potassium channels in vascular smooth muscle cells and adrenergic nerve receptors. These factors increase endothelium-dependent vasodilation, thus decrease blood pressure (Haddy et al., 2006). b) increased serum potassium is also associated with increases in sodium excretion, modulation of baroreceptor sensitivity, reduced sensitivity to catecholamine related vasoconstriction, improved insulin sensitivity and decreases in oxidative stress and inflammation (Houston, 2011).

The mechanisms of how sodium effects blood pressure are: High sodium inhibit the sodium pump, increase intracellular sodium and drive calcium into cells (Adrogue and Madias, 2007). In this situation, vascular smooth muscles contraction and peripheral vascular resistance are increased. The effect of sodium was reported to be related with gene. Many "salt-sensitive" individual genes influence the body's handling of sodium to varying degrees, therefore, in most cases, essential hypertension is a genetic disorder (Ji et al., 2008).

Four observational studies were found exploring the association between dietary potassium intake and blood pressure. Three of them are cross-sectional studies (Chmielewski and Carmody, 2017, Smith and Franzen-Castle, 2012, Campanozzi et al., 2015), where the participants' age ranged from 6 to 18 years, the sample size ranged from 335 to 4716. The dietary potassium intake was assessed by interview, 24-h dietary recall or 24-h urine test. The other study is longitudinal (Buendia et al., 2015), the participants were 2185 girls aged 9 to 10 years. Three-day dietary record was used to assess diet.

No relationship between dietary potassium intake and blood pressure was found in two cross-sectional studies (Chmielewski and Carmody, 2017, Smith and Franzen-Castle, 2012). But in the other cross-sectional study (Campanozzi et al., 2015), although diet was not measured directly, Campanozzi found 24-h urinary potassium excretion was linked with higher SBPZ. In the longitudinal study (Buendia et al., 2015), an opposite result was found. Potassium intake was linked with lower SBP and DBP change throughout adolescence period.

Five studies were found exploring the association between dietary sodium intake and blood pressure. Three of them are cross-sectional studies (Chmielewski and Carmody, 2017, Smith and Franzen-Castle, 2012, Campanozzi et al., 2015), where the participants' age ranged from 6 to 18, the sample size ranged from 335 to 4716. The dietary sodium intake was assessed by interview, 24-h dietary recall or 24-h urine test. The other two of the five studies are longitudinal studies (Buendia et al., 2015, Setayeshgar et al., 2017a), where the participants' age ranged from 9 to 19 years, and the sample size ranged from 448 to 2185. Both of them used dietary record to measure diet.

In two of the cross-sectional studies (Chmielewski and Carmody, 2017, Smith and Franzen-Castle, 2012) and one of the longitudinal study (Buendia et al., 2015), no significant association was found between sodium intake and blood pressure. But in the other cross-sectional study (Campanozzi et al., 2015) and the longitudinal study (Setayeshgar et al., 2017a), positive association was found. The cross-sectional study found association between higher 24-h urinary sodium excretion and increased SBPZ, after adjusting for age and BMI (Campanozzi et al., 2015). The longitudinal study found a positive association between sodium intake at base line and DBPZ increase between baseline and the follow-up (Setayeshgar et al., 2017a).

Two studies explored potassium to sodium ratio (Buendia et al., 2015, Chmielewski and Carmody, 2017). Both of them found negative association between potassium to sodium ratio and systolic blood pressure.

1.4.5 Association between blood pressure and main food groups

Salt and salty food

Three observational studies were found about dietary salt intake and blood pressure. Two of them are cross-sectional studies (Jayashri et al., 2015, Woodruff et al., 2014) , where participants' age ranged from 10 to 19 years, and sample size ranged from 435 to 495. Questionnaires (Jayashri et al., 2015, Woodruff et al., 2014) were used in both of these two studies to measure salt intake. In woodruff's study, a food behaviour questionnaire was used to measure salt intake, but using of table salt was not taken into consideration, therefore the observed total salt intake could be lower than actual value. The other study is longitudinal (Shi et al., 2014), where the participants' age ranged from 4 to 18, and sample size is 435. Dietary records were used to collect diet data .

One of the cross-sectional study (Woodruff et al., 2014) found no association between salt intake and blood pressure in univariate analyses, with no factors adjusted. Therefore, the result might be biased by ignoring potential confounders. Positive association was found in other cross-sectional study and the longitudinal study. In the longitudinal study (Shi et al., 2014), after adjusting for BMI-SDS (Standard Deviation Score), height-SDS, growth velocity, physical activity, total energy intake, Ca and Mg intakes, maternal overweight (BMI kg/m^2) and education levels as well as the early-life factors (including birth weight, gestational age and breast-feeding status), a 1 g/day increase in salt intake was related with a 0.2 mmHg increase in SBP.

Three cross-sectional studies explored the association of salty food and blood pressure. The participants' age ranged from 6 to 19 years, and sample size ranged from 424 to 1200. Two of them (Asghari et al., 2016, Ponzo et al., 2015) found higher salty snacks intake was linked with higher blood pressure values or higher risk of hypertension, the other (Jayashri et al., 2015) found positive association between pickle intake and blood pressure levels.

Fruit and Vegetable

Six observational studies were found. Four of them are cross-sectional (Heidari-Beni et al., 2015, Kim et al., 2017, Prasad et al., 2017, Payab et al., 2016), where participants' age ranged from 6 to 18 years, and sample size ranged from 205 to 136739. All of them used FFQ to assess diet. The other two of the six studies are longitudinal, where

participants' age ranged from 4 to 19 years, sample size ranged from 435 to 438. Both of them used dietary record to assess diet.

Conflicting results were found in these studies. In cross-sectional studies, Prasad found low fruit diet was linked with raised risk of high blood pressure, but no significant was found with vegetable intake and risk of high blood pressure (Prasad et al., 2017). While the other two studies found no significant association between fruit and vegetable intake and SBP and or DBP (Kim et al., 2017, Payab et al., 2016), and Heidari-Beni found potato consumption was not linked with blood pressure levels in 11 to 13 years old girls (Heidari-Beni et al., 2015). A longitudinal study (Setayeshgar et al., 2017a) found vegetables and fruit intake was not associated with change in BP levels during 2 years' follow up, and the other longitudinal study (Shi et al., 2014) found that after adjusting for BMI-SDS (standard deviation score), height-SDS, growth velocity, physical activity, total energy intake, Ca and Mg intakes, maternal overweight, and BP and education levels as well as the early-life factors (including birth weight, gestational age and breast-feeding status), a negative of fruit and vegetable intake (FVI) with blood pressure was found: every 100 g/day lower FVI was related to a 0·4mmHg higher blood pressure.

Nuts and seeds

One cross-sectional study (O'Neil et al., 2012) was found exploring the association between "out-of-hand" nut consumption and blood pressure. The study contains children, adolescents and adults participants. "Out-of-hand" nuts were defined as those nuts consumed solely as nuts and not as part of products, for example, in breads, cereals, or candy bars. Adult "out-of-hand" nuts consumers also had a 19% decreased risk of hypertension, but no relationship was found in adolescents.

An interventional study (Machado et al., 2015) was found exploring the impact of flaxseed intake on blood pressure in overweight adolescents. It is a single-blind clinical trial. The participants were randomized into brown flaxseed group, golden flaxseed group or control group. Participants received 28 g/d brown flaxseed, golden flaxseed or wheat bran from Monday to Friday for 11 weeks. At the end of the study, participants who received brown and golden flaxseed had significant lower DBP.

Dairy

Three cross-sectional studies (DellaValle et al., 2017, Kim et al., 2017, Smith and Franzen-Castle, 2012) were found. The participants' age ranged from 4 to 18 years, and sample size ranged from 117 to 136739. Two of them used FFQ and one used 24-hour diet recall to collect diet data. Conflicting results were reported.

Smith found per unit of dairy intake was associated with 4.82 mmHg decrease in girls' DBP but not with boys (Smith and Franzen-Castle, 2012). DellaValle found a negative association between dairy intake and SBP in total sample and white participants, but not in black participants (DellaValle et al., 2017). Kim found no association between dairy intake and blood pressure levels (Kim et al., 2017).

Sugar-sweetened beverages (SSB)

Four cross-sectional studies were found (Ambrosini et al., 2013, Loh et al., 2017, Souza et al., 2016, Chan et al., 2014). Their participants' age ranged from 8 to 18 years old, and sample sizes ranged from 488 to 2727. Three of them used FFQ (Ambrosini et al., 2013, Chan et al., 2014, Souza et al., 2016), and the other used questionnaire to collect dietary data (Loh et al., 2017). Three of them found positive associations between sugar-sweetened beverages and blood pressure levels (Ambrosini et al., 2013, Chan et al., 2014, Souza et al., 2016), the other found a U-shaped association (Loh et al., 2017). Souza (Souza et al., 2016) found diet soft drink consumer had higher SBP and DBP compared with non-consumers and sugar-sweetened consumers.

1.4.6 Association between blood pressure and dietary patterns

Three cross-sectional studies were found about effects of different dietary patterns on blood pressure in adolescents. Participants' age ranged from 12 to 25, and sample size ranged from 487 to 1319.

In 1019 fifteen to sixteen aged adolescents, a modern dietary pattern (Aounallah-Skhiri et al., 2011), stands for increased consumption of white bread, dairy products, sugars, added fats and fruits and decreased consumption of oils, grains, legumes and vegetables, while decreased total fat, vitamin C, potassium, fibre and increased calcium, energy, sugars and saturated fat intake, was associated with decreased prevalence of hypertension, adjusted for BMI and waist circumference. The diet data was collected using 24-hour diet recall. This effect might be caused by higher intake of fruits and

lower intake of oils, or as a result of inadequate adjustment for potential confounders like alcohol intake, etc.

Animal protein pattern (Mu et al., 2014) was defined as high loadings for pork, mutton, beef, poultry meat and animal live. It was found to be associated with increased risk of elevated blood pressure among 1319 sixteen to eighteen years old Chinese adolescents, after adjusting for sex, physical activity, economic status, passive smoking, drinking, and BMI. The diet data was collected using FFQ.

Sweet tooth dietary pattern (McCourt et al., 2014) was characterised by the highest factor loadings for puddings, chocolates and confectionery, was reported to be linked with increased systolic blood pressure and diastolic blood pressure, after adjusting for age (years), sex, BMI (kg/m2), social status, physical activity, smoking status and energy (kJ). Diet data was obtained using the diet history method.

1.4.7 Summary of the results of previous studies

The summary of the results are displayed in Table 1.4 . For most of the nutrients, conflict results were found in their association with blood pressure.

Table 1.4 Summary of the results of previous studies

Nutrients	Number of studies reported the association between dietary factors and blood pressure			
	Positive	None	Negative	U-shape
Energy	2	1	0	0
Carbohydrate	2(GI/GL)	1(fructose)	2	0
Fat	2	1	0	0
Protein	0	1	2	0
Fibre	0	1	1	0
Magnesium	0	1	0	0
Calcium	1	0	2	0
Potassium	1	2	1	0
Sodium	2	3	0	0
Potassium /Sodium	0	0	2	0
Salt and salty food	4	1	0	0
Fruit and vegetable	1(fruit)	3	0	0
Nut and seed	0	1(nuts)	1(flaxseed)	0
Dairy	0	2	2	0
SSB	3	0	0	1
Vitamins	0	0	0	0

1.5 Discussion

Prevalence of hypertension in adolescents is increasing, and higher blood pressure levels in childhood and adolescenthood is a strong predictor of adult hypertension. Diet is among the most important factors that influence blood pressure.

1.5.1 Summary of results

Thirty-two papers were found in this literature review. Most of them are cross-sectional observational studies (81.3%), while longitudinal studies (12.5%) and trials (6.3%) are less common. In the observational studies, the majority used FFQ to assess diet (43.3%), followed by dietary recall (20.0%), dietary record (20.0%) and questionnaire (16.7%). One study used 24-h urine test to indicate dietary sodium and potassium intake.

1.5.2 Macronutrients and blood pressure

Higher energy, total fat intake were mainly linked with increased blood pressure levels, while higher protein and total carbohydrate were mainly linked with decreased blood pressure levels. Intake of long chain omega-3 fatty acids from fish oils was reported to increase blood pressure (Xun et al., 2011) or have no effects (Root et al., 2013) on blood pressure in adults, and DHA was reported to increase systolic blood pressure (Lauritzen et al., 2012) in adults. But no relevant study among adolescents was identified. No significant relationship between diet fructose intake and blood pressure was found, but fructose intake was related with serum uric acid, which was reported to positively related with systolic blood pressure. Higher intake of high GI/GL foods were linked with higher blood pressure levels.

1.5.3 Minerals and blood pressure

Association between minerals and blood pressure were conflicting. Only higher potassium to sodium ratio was linked with lower blood pressure. One study of magnesium found no significant relationship, but in a literature review (Simons-Morton and Obarzanek, 1997), 5 studies about diet magnesium intake and blood pressure among children or adolescents were reported. Four of them reported inverse relationship between dietary magnesium and blood pressure, while the other found no significant result. However, three of these five studies had participants under 10 years old, and the other two studies were not analyzed with current and appropriate statistical methods as they are such old papers. Review of adult studies showed similar results on magnesium

(Mizushima et al., 1998). The results on calcium are conflicting. The found were similar to a previous review (Simons-Morton and Obarzanek, 1997), where 5 studies were included, of which 2 found negative relationship and 3 found no relationship between dietary calcium intake and blood pressure. In the current review, the results of potassium were also conflict. In the previous review (Simons-Morton and Obarzanek, 1997), four studies were included, two reported significant inverse association, the other two found no association. Within these studies there is a cross-sectional study (Liebman et al., 1986) of 14-year-old girls, sample size is 532. Two 24-hour diet recall was used to collect diet data. After adjusting for family per capita income level, anthropometric and dietary variables, age at menarche, potassium intake was reported to have a negative relationship with blood pressure. In the current review, two studies found sodium intake was positively linked with blood pressure levels, but 3 found no association. In the previous review (Simons-Morton and Obarzanek, 1997), 4 studies that controlled confounders were reported. Three of the four studies found positive relationships between sodium intake and blood pressure, and the other found no relationships.

1.5.4 Vitamins and blood pressure

No studies exploring the association between dietary vitamin intakes and blood pressure in adolescents were found, however vitamins were found to be linked with cardiometabolic health and blood pressure levels in adult studies and studies earlier than the year of 2011. Two studies had studied vitamin D. One cross-sectional study focused on diet vitamin D and cardiometabolic risk score (Moreira et al., 2014). The participants are Azorean adolescents, age range from 15 to 18 years old, and the sample size is 496. A semi-quantitative FFQ was used to collect diet data. After adjusting for total energy intake, pubertal stage, fat mass percentage, and cardiorespiratory fitness, an increased vitamin D intake was associated with lower cardiometabolic risk score, which was related with blood pressure. However no evidence of vitamin D intake and blood pressure was found. The other one is a cross-sectional study (Rafraf et al., 2014), the participants' age range from 14 to 17 years old, and sample size is 216. This study reported no relationship between serum vitamin D and blood pressure. Sun exposure data was not adjusted in both studies, therefore the reliability of the results is limited. One cross-sectional study was found to explore the relationship between folate and blood pressure in adolescent in the year of 2000 (Falkner et al., 2000). The participants are 14 to 16 years old hypertensive adolescents, and the sample size is 180. A 24-hour

diet recall was used to collect diet data. The mean diastolic blood pressure of low folate group was significantly higher compared to the high folate group (boys: 72 vs. 67 mmHg; girls: 76 vs. 73 mmHg; P =0.008), but thus result was not found in systolic blood pressure. However, data were analysed by 2-way analysis of variance, not fully adjusted for potential confounders. A 20-year longitudinal study among adults (Xun et al., 2012) also found a negative relationship between dietary folate and hypertension after adjusting for several confounders. However the effect of diet folate on blood pressure was still not clear based on existing evidence.

1.5.5 Dairy and blood pressure

In the current review, two studies found dairy intake was linked with lower blood pressure, and two found no association. Different types of dairy products might have different effects on blood pressure, as a result of their different composition. A more detailed study, with intake of sub-groups of dairy as exposures, and adjusted for sufficient confounders such as dietary energy, fat intake, calcium intake, physical activities should be done to clarify the association between dairy intake and blood pressure in adolescents.

1.5.6 Sugar-sweetened beverage and blood pressure

Sugar-sweetened beverage was found to be associated with increased blood pressure in 3 studies, while a U-shaped association was found in the other study. Sugar and sweets intake was also found to be linked with blood pressure levels. One cross-sectional study (Fasting et al., 2008) was found about relationship between sweet intake and blood pressure in adolescents. The participants' age ranged from 13 to 19, sample size is 8408. Sweet intake was measured by frequency, the classifications are "once per day or more", "every week, but not every day" and "less than once per week". Results shown that both girls and boys with higher frequency of sweets intake had lower systolic blood pressure (both p for trend <0.001), both girls and boys with higher frequency of sweets intake had lower diastolic blood pressure (p for trend=0.02 for girls, 0.03 for boys), boys with higher frequency of sweets intake had lower SBP (p<0.001) but no significant result was found in multiple regression. This result might be biased for ignoring the effect of potential confounders like energy intake, fat intake, BMI, physical activities, etc.

1.6 Conclusion

Further good quality studies are needed to clarify the association between diet and blood pressure in adolescents. More longitudinal and interventional studies are needed. Dietary record method should be used rather than dietary recall or FFQ. In statistical analysis, potential confounders should be adjusted properly.

Chapter 2. Dietary factors and blood pressure in UK adolescents: finding from National Diet and Nutrition Survey (cross-sectional)

Abstract

Backgrounds: Studies supported that diet could affects blood pressure levels, but epidemiological evidences are needed to confirm the association among adolescents. The aim of this study is to determine the relationship between dietary vitamin E and fats intake and blood pressure in 10-19 years UK adolescents.

Methods: 10-19 years old adolescents were selected from the UK National Diet and Nutrient Survey in which sample was drawn randomly. General information was collected from interview, anthropometric data and BP were measured, and dietary data was assessed from a four-day food record. BP data was transformed to systolic BP Z-scores (SBPZ) and diastolic BP Z-scores (DBPZ). Univariable and multivariable linear/logistic regression was undertaken for continuous outcomes (Z-scores)/binary outcomes (hypertension vs. normal BP). In the final models, age, gender, alcohol intake, smoking, ethnicity, household income, sugar sweetened beverage intake, total fruit and vegetable intake, sodium intake and energy intake were adjusted.

Results and Conclusion: In the NDNS adolescent population, the prevalence of hypertension was 7%. Higher dietary vitamin E intake was found to have associations with lower systolic blood pressure, lower systolic blood pressure Z-scores and lower risk of hypertension. Higher dietary trans-fatty acids was linked with higher SBP and higher SBPZ. Higher dietary polyunsaturated low fat spread intake was linked with higher SBP. Higher serum total cholesterol was associated with higher SBP and SBPZ.

2.1 Introduction

2.1.1 Diet intake and blood pressure

To determine risk factors of elevated blood pressure is the prerequisite of prevention. According to Guidelines for Management of Hypertension published by the British Hypertension Society in 2004 (Williams et al., 2004), many risk factors had been reported to elevate blood pressure in adults, like obesity, lack of physical activities, cigarette smoking, alcohol intake, highly intake of salt and fat. Other factors like family history (Muldoon et al., 1993), social economic status (Colhoun et al., 1998, Krieger et al., 2014) and ethnicity (Gasevic et al., 2015, Piper et al., 2014, Krieger et al., 2014) had also been proved to affect blood pressure. In adolescents, some same factors were found to affect blood pressure, include obesity (Wong et al., 2013, Kelishadi et al., 2013, Sugiyama et al., 2007), smoking and passive smoking (Huntington-Moskos et al., 2014, Hacke and Weisser, 2015, Giussani et al., 2013), alcohol intake (Zhang et al., 2013, Riley and Bluhm, 2012), lack of physical activities (So et al., 2013, Yoshinaga et al., 2011, Sugiyama et al., 2007, Pahkala et al., 2012, Dennison, 2012), family history (Xu et al., 2015, Westerdahl et al., 2013), social economic status (Kaczmarek et al., 2015, Griffiths et al., 2012), ethnicity (Noor et al., 2013, Fang et al., 2012, Hemmings et al., 2011a, Hemmings et al., 2011b, Harding et al., 2006) and dietary factors (Sugiyama et al., 2007), etc.

Among all the dietary factors, vitamin E and fats intake are two of the most important factors that influence blood pressure levels in adolescents, and were chosen to be analysed in this study. The choice was made based on the current study background and the raw analysis of the NDNS dataset. In the literature review of Chapter 1, several gaps were found in the current literature, including the conflicting results between adults and adolescents in fats, and the lack of studies in the area of vitamins.

Vitamin E

Vitamin E is a group of potent, lipid-soluble antioxidants. Molecules having vitamin E antioxidant activity include α-, β-, γ-, δ-tocopherols and α-, β-, γ-, δ- tocotrienols (Brigelius-Flohe and Traber, 1999). Many studies support the view that vitamin E has the potential to reduce the risk of hypertension because of its antioxidant and anti-inflammatory affects (Reiter et al., 2007, Rodrigo et al., 2008, Kromhout, 2001, Jiang, 2014). Vitamin E intake was found to increase total serum antioxidant capacity as it could act as a chain breaking factor to reduce the production of plasma oxidative

markers such as LOOH. High concentrate of LOOH can destroy the cell membrane, reduce the compliance of the arteries and then cause high blood pressure (Plantinga et al., 2007). Also the antioxidant effect of serum tocopherol was found to preserve endothelial vasomotor by protecting nitric oxide (Plotnick et al., 1997, Boger et al., 1998, Kinlay et al., 1999) or increasing the releasing of nitric oxide in platelets (Freedman et al., 1996). Thirdly, tocopherol was found to inhibit the function of regulators that are involved in activation and transcription of several proteins that are key in the inflammatory process, such as protein kinase C (PKC) (Venugopal et al., 2002, Tasinato et al., 1995, Reiter et al., 2007), Akt (Kempna et al., 2004) and NFκB (Li et al., 1999, Sury et al., 2006, Suzuki et al., 1993). When inflammation persists, the vasomotor effect of nitric oxide decreases, so that blood vessels relax and vasodilatation is absent (Agita and Alsagaff, 2017). Tocopherol, especially α-tocopherol can help prevent the absence of vasodilation due to its anti-inflammatory affects.

However, the impact of dietary vitamin E intake on blood pressure reported in several adult epidemiologic studies have inconsistent results (Boshtam et al., 2002, Llopis-Gonzalez et al., 2015). Few studies have investigated the association between dietary vitamin E intake, serum tocopherols and blood pressure in children and adolescents. One longitudinal study (Mishra et al., 2003) in the UK found lower consumers of vitamin E in both childhood and adulthood were more likely to be hypertensive as adults (OR =1.8, 95%CI: 1.03 to 3.08), but a low intake of vitamin E at just one time point in either childhood or adulthood was not associated with a statistically significant increased risk of hypertension. Little evidence on the association between vitamin E status and blood pressure in adolescents has been found in previous studies.

Fats

Fats are esters of three fatty acid chains and the alcohol glycerol. Dietary fats intake, including saturated fatty acid (SFA), monounsaturated fatty acid (MUFA) and polyunsaturated fatty acid (PUFA), had been studied on their influence on blood pressure (Rees et al., 2013, Schwingshackl et al., 2011, Cabo et al., 2012, Xun et al., 2011, Root et al., 2013, Lauritzen et al., 2012).

Total fat intake, SFA and TFA might contribute to increased blood pressure by increasing inflammatory and oxidative stress (Ruparelia et al., 2017, Sverdlov et al., 2016, Longhi et al., 2018, Munoz and Costa, 2013). However, unsaturated fatty acids, especially omega-3 fatty acids were found to be linked with lower blood pressure in

adults. As discussed in Chapter 1, endothelial dysfunction is a cause of hypertension, which is involved with lower nitric oxide level and inflammation (Nestel, 2019). Long-chain omega-3 fatty acids was found to improve the endothelial function by increasing nitric oxide level (Wang et al., 2012, de Roos et al., 2009) and reducing circulating concentrations of inflammatory biomarkers (Allaire et al., 2016, Pase et al., 2011). Therefore, it may improve the function of endothelial tissue. Long-chain omega-3 fatty acids were also found to have an effect on lowering arterial stiffness in both large and small arteries (Nestel et al., 2002, Mori and Woodman, 2006).

In children and adolescents, both observational studies and randomized controlled trial were found exploring the relationship between dietary fats intake and blood pressure. Total fat (Aeberli et al., 2009, Mirza et al., 2013, Setayeshgar et al., 2017b), MUFA (Aeberli et al., 2009, Sugiyama et al., 2007) and total cholesterol (Ventura et al., 2008) intake were found to be linked with increased blood pressure, while SFA (Aeberli et al., 2009, Post et al., 1997) intake was found to be linked with decreased blood pressure. The results were rare and conflicted to the conclusion in adults, where MUFA were recommended to reduce the risk of hypertension (Schwingshackl et al., 2011).

Contradictory results from previous studies on the association between dietary vitamin E, fats intake and blood pressure support the needs to carry out further study on this topic.

2.2 Aims

The aims of this study are to determine the cross-sectional relationships between

a. dietary vitamin E intake, serum tocopherols and blood pressure and
b. dietary fats intake, serum lipids profile

in UK adolescents aged 10-19 years, according to National Dietary and Nutrition Survey (NDNS) 2008-2014.

2.3 Methods

2.3.1 Sample

Adolescents were sampled from the NDNS 2008-2014. The NDNS is a national nutrition survey in the UK. It was designed to assess the diet, nutrient intake and nutritional status of the general population living in private households in the UK. Participants were recruited randomly from the Postcode Address File each year for 6 years since 2008. All adolescents who met the following inclusion criteria were

included in the analyses: adolescents who were 10 to 19 years old, who had no missing values in dietary data and blood pressure data. Adolescents who were taking any drugs to control blood pressure were excluded from the current study.

2.3.2 Ethical approval

Ethical approval for the NDNS was obtained from the Oxfordshire Research Ethics Committee(Public-Health-England and Food-Standards-Agency, 2014). All of the participants were informed about the survey and gave consent before recruitment. For adolescents aged under 16 years, both the adolescent's and their parent's (or guardian's) consent were obtained.

2.3.3 Data collection

In the NDNS, the following data were collected: dietary data, general information, smoking habits, blood samples, measurements of weight and height and blood pressure. General information was collected from a face-to-face Computer Assisted Personal interview (CAPI). Smoking habits were collected from a Self-completed Questionnaire. Dietary data were derived from a self-completed 4-day dietary diary, and a parent was asked to keep the food diary on behalf of participants aged 11 years and under. Blood samples were collected after an overnight fast by a nurse. Weights and heights were measured by trained interviewers using a standard protocol.

Blood pressure was measured using a standard protocol by a trained nurse using a validated blood pressure monitor (Omron HEM-907). The cuff size was chosen according to the participant's mid upper arm circumference: 15-22cm for small cuff, 22-32cm for medium cuff and 32-42cm for large cuff. Cuff was attached to the participant's right arm. Participants was asked to sit quietly for 5 minutes before the measurement and during the measurement. Arm position was not mentioned in the NDNS protocol. Three measurements were taken with one minute intervals between each measurement. Results were based on the mean of the second and third readings.

2.3.4 Data analysis

Data transformation

Energy and nutrient intake (with and without supplements) were calculated based on the food consumption data from dietary record. Alcohol intake was collected from dietary record as well. Smoking status was transformed to a YES/NO variable as different questions were asked in different age groups. YES represented 10-15 year olds whose

answer to the frequency of smoking was “more than once a week” or “once a week and less”, and in 16-19 year olds whose answer to the question “Do you smoke now” was “Yes”. While NO represented 10-15 year olds whose answer to the frequency of smoking was “No” and for 16-19 year olds whose answer to the question “Do you smoke now” was “No”. Obesity status was defined as norman (BMI<85th centile), overweight (85th -95th centile) and obese (over 95th centile). Social economic status was described using equivalised household income.

Blood pressure and blood pressure Z-scores

Blood pressure values from three measurements were recorded, and the mean of the last two results were calculated for the final analysis. In adolescents aged 10-17 years, both their SBP and DBP were transformed to systolic and diastolic blood pressure Z-scores (SBPZ and DBPZ), using age, gender and height data, according to the “Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents(NHBPEP-working-group, 2004)”, as recommended by the European Hypertension Society.

Hypertension in children and adolescents under 18 years old is defined as SBP and/or DBP ≥95th percentile (equals to Z-score ≥1.645). Hypertension in 18 and 19 year old adolescents is defined as SBP ≥140 mmHg and/or DBP ≥90 mmHg. The definition was based on Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents(NHBPEP-working-group, 2004) and the British Hypertension Society Guidelines (Williams et al., 2004).

2.3.5 Statistical analysis

STATA/SE 13.1 for Windows was used to conduct all the statistical analysis. The level of statistical significance was <0.05. All data were generally normally distributed, therefore data was described using mean and standard deviation. T-tests were used to compare energy intake, nutrients intake, serum tocopherols, serum lipids between hypertensive and non-hypertensive adolescents. Raw analysis was done to explore the association between blood pressure levels and all the nutrients. Potential factors (vitamin E and fats intake) that could have relations with blood pressure were selected based on the result. The relationships between dietary vitamin E intake (with or without supplements) and serum tocopherols, between dietary fats intake and serum lipids were tested using linear regression.

Preliminary analysis

Energy or each nutrient intake with supplements was included in the analysis as exposure separately. Linear regression for continuous outcomes (SBPZ and DBPZ) was undertaken to explore the associations. In addition, logistic regression for binary outcomes (hypertension vs. normal blood pressure) was undertaken. For each exposure and outcome, one univariable model (Model 1) and one multivariable model (Model 2) adjusting for different confounders were created. Confounders were selected according to a specifically designed Directed Acyclic Graph (DAG) (Figure 2.1) and previous studies.

The confounders in each model were:

Model 1 (M1): unadjusted.

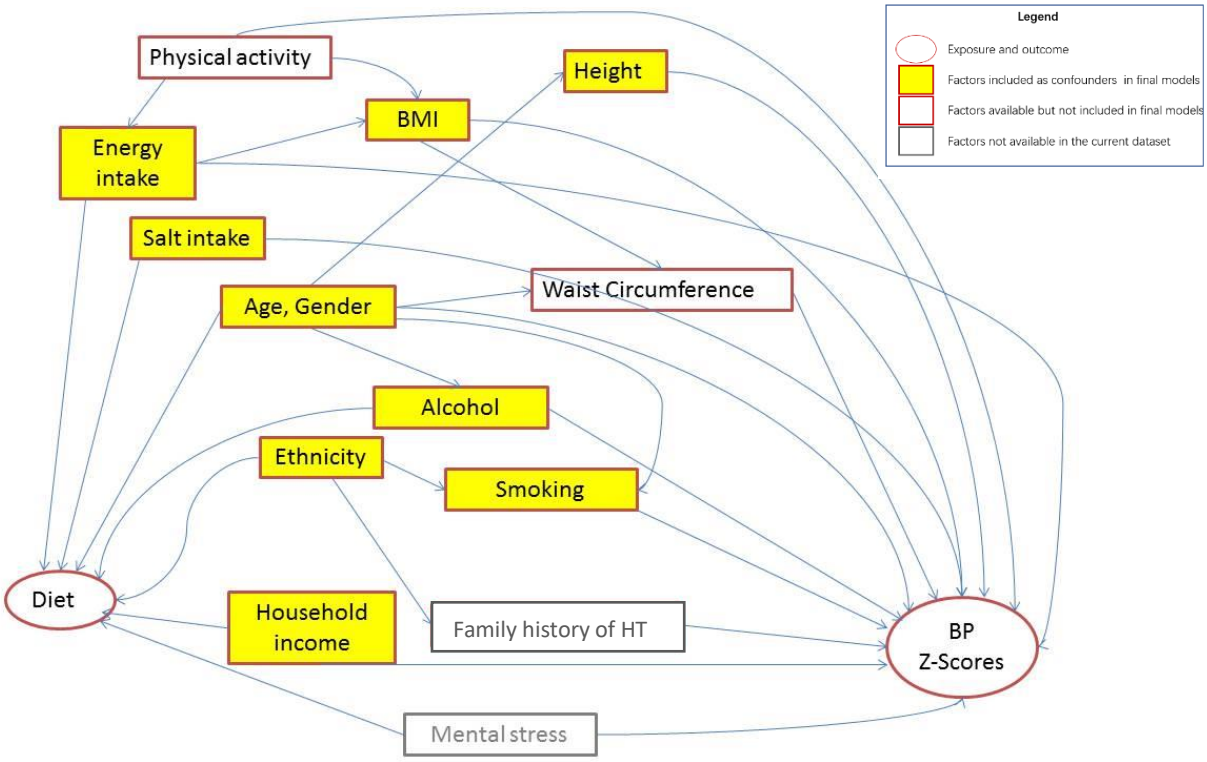
Model 2 (M2): adjusted for age, sex, smoking status, alcohol consumption, dietary energy intake, dietary sodium intake and social economic status.

Based on the results of the preliminary analysis, dietary factors that could potentially have an association with blood pressure levels were selected for further analysis.

Associations between vitamin E levels, fat levels and blood pressure

Linear regression for continuous outcomes (SBP, DBP, SBPZ and DBPZ) was undertaken to explore the associations. In addition, logistic regression for binary outcomes (hypertension v.s. normal blood pressure) was undertaken. For each exposure and outcome, one univariable model (Model 1) and one multivariable model (Model 2) adjusting for different confounders adjusted were created. Confounders were selected according to a specifically designed Directed Acyclic Graph (DAG) (Figure 2.1) and previous studies.

Figure 2.1 Directed Acyclic Graph (DAG) of the NDNS analysis



The confounders in each model were:

Model 1 (M1): unadjusted.

Model 2 (M2): adjusted for age, sex, ethnicity, BMI category, height, smoking status, alcohol consumption, dietary energy intake (dietary energy intake except fats was included instead of total energy in models which fats intake and serum lipid profile was exposures), dietary sodium intake, and social economic status were adjusted in final models.

The exposure factors were:

a. Dietary vitamin E intake: diet only (g) or with supplements (g)
b. Serum tocopherols: α-tocopherols (µmol/l) and serum γ-tocopherols (µmol/l)
c. Dietary fats intake: fat (g), saturated fatty acids (g), unsaturated fatty acid (g), cis-monounsaturated fatty acids (g), cis n-3 fatty acids (g), cis n-6 fatty acids (g), trans fatty acids (g), low fat spread not polyunsaturated (g), low fat spread polyunsaturated, reduced fat spread not polyunsaturated (g), reduced fat spread polyunsaturated (g), other margarine, fats and oils (g)

d. Dietary fats intake count for total energy: fat percent total energy, saturated fatty acids percent total energy, cis monounsaturated fatty acids percent total energy, cis n3-polyunsaturated fatty acids percent total energy, cis n6-polyunsaturated fatty acids percent total energy, trans fatty acids percent total energy
e. Serum lipid profile: total cholesterol (mmol/l), triglycerides (mmol/l), high density lipoproteins (mmol/l), low density lipoproteins (mmol/l)

The outcome factors were:

a. Blood pressure values: systolic blood pressure, diastolic blood pressure
b. Blood pressure Z-scores: systolic blood pressure Z-scores, diastolic blood pressure Z-scores
c. Risk of hypertension

2.4 Results

2.4.1 General information

The rate for children/adolescents who completed the diet records was 56% in year 2008-2012 (Public-Health-England and Food-Standards-Agency, 2014) and 53% in year 2012-2014 (Public-Health-England and Food-Standards-Agency, 2016). Total sample of 10 to 19 year old adolescents was 2345. 966 of them were excluded due to missing blood pressure values. 1379 met all the inclusion criteria (699 males and 680 females). General information was generally comparable between samples missing blood pressure values and samples with valid blood pressure values. See Table 2.1.

Table 2.1 General Information

Items	Total	Samples missing blood pressure	Samples with valid blood pressure		
			Total	Non-hypertensive group	Hypertensive group
N	2345	966	1379	1282	97
Gender(Male/Female)	1169/1176	489/477	680/699	618/664	63/53
Age (Mean±SD)	14.2±2.6	14.2±2.6	14.1±2.6	14.2±2.6	13.6±2.5
Ethnicity [n(%)]					
White	1578(63.7%)	642(66.5%)	936(67.9%)	872(68.0%)	64(66.0%)
Other groups	149(6.4%)	78(8.1%)	71(5.1%)	64(5.0%)	7(7.2%)
Missing	618(26.4%)	246(25.5%)	372(27.0%)	346(27.0%)	26(26.8%)
Total household income in last 12 months [n(%)]					
Under £20,000	742(31.6%)	328(34%)	414(30%)	379(29.6%)	35(36.1%)
£20,000-£34,999	497(21.2%)	207(21.4%)	290(21%)	265(20.7%)	25(25.8%)
£35,000-£44,999	348(14.8%)	128(13.3%)	220(16%)	207(16.1%)	13(13.4%)
£50,000 or more	453(19.3%)	160(16.6%)	293(21.2%)	283(22.1%)	10(10.3%)
Missing	305(13%)	143(14.8%)	162(11.7%)	148(11.5%)	14(14.4%)

65

Alcohol Intake [n(%)]					
Yes	720(30.7%)	299(31%)	421(30.5%)	337(26.3%)	21(21.6%)
No	592(25.2%)	235(24.3%)	357(25.9%)	400(31.2%)	20(20.6%)
Missing	1033(44.1%)	432(44.7%)	601(43.6%)	545(42.5%)	56(57.7%)
Alcohol Intake (ml, Mean±SD)	17.2±22.2	18.8±20.5	16.4±23.1	19.6±23.3	32.5±45.9
Smoking [n(%)]					
Yes	218(9.3%)	125(12.9%)	93(6.7%)	90(7.0%)	3(3.1%)
No	1415(60.3%)	557(57.7%)	858(62.2%)	796(62.1%)	62(63.9%)
Missing	712(30.4%)	284(29.4%)	428(31%)	396(30.9%)	32(33.0%)
Height(cm, Mean±SD)	161.4±12.7	161.4±12.8	161.5±12.6	161.5±12.6	160.5±12.8
Weight(kg, Mean±SD)	57.1±16.5	56.9±16.8	57.2±16.4	56.8±15.9	63.5±21.7
Systolic Blood Pressure (mmHg, Mean±SD)					
	-	-	-	109.9±9.7	129.8±11.6
Diastolic Blood Pressure (mmHg, Mean±SD)					
	-	-	-	62.0±8.1	73.7±11.5
Prevalence of Hypertension in total sample [n(%)]					
Yes	-	-	97(7.0%)	-	-
No	-	-	1282(93.0%)	-	-

2.4.2 Blood pressure levels and prevalence of hypertension

7.0% (95%CI: 5.7% to 8.4%) of them were defined as hypertensive. Mean systolic blood pressure was 109.9±9.7 mmHg in normotensive adolescents, and was 129.8±11.6 in hypertensive adolescents. Mean diastolic blood pressure was 62.0±8.1 mmHg in normotensive adolescents, and was 73.7±11.5 in hypertensive adolescents. See Table 2.1.

Prevalence of hypertension slightly dropped from 8.1% to 7.3% during the six years. In year 4 the prevalence was the lowest (4.8%, see Table 2.2.a). Prevalence in Wales adolescents was the highest among all the four countries (11.3%, see Table 2.2.b).

Table 2.2.a Prevalence of hypertensive adolescents in each survey year (2008 -2014)

	2008-2009	2009-2010	2010-2011	2011-2012	2012-2013	2013-2014
Normotensive % (N)	91.9% (216)	91.8% (246)	93% (238)	95.2% (236)	93.4% (156)	92.7% (190)
Hypertensive % (N)	8.1% (19)	8.2% (22)	7% (18)	4.8% (12)	6.6% (11)	7.3% (15)
Total (N)	235	268	256	248	167	205

Table 2.2.b Prevalence of hypertensive adolescents in each country

	England	North Ireland	Scotland	Wales
Normotensive % (N)	93.7%(680)	94%(202)	92.7%(266)	88.7%(134)
Hypertensive % (N)	6.3%(46)	6%(13)	7.3%(21)	11.3%(17)
Total (N)	726	215	287	151

2.4.3 Energy and nutrients intake

Normotensive adolescents had lower values compared to hypertensive adolescents for daily total energy intake (1764.02±499.59 kcal/day v.s. 1821.40±489.13 kcal/day, p=0.473) and sodium intake (2230.63±794.54 mg/day v.s. 2377.01±736.55 mg/day, p=0.250] respectively, although without statistically significant. No significant difference was found of vitamin E intake and serum tocopherols between normotensive and hypertensive adolescents. Normotensive adolescents had higher values compared to hypertensive adolescents for daily polyunsaturated low fat spread intake (0.72±3.30 g/d v.s. 0.32±1.45 g /day, p=0.432) and lower value of low fat not polyunsaturated intake (0.17±1.04 g/d v.s. 0.86±3.65 g /day, p=0.002). See Table 2.3.

Table 2.3 Daily energy intake, nutrient intakes, serum tocopherol and serum lipid profile

Nutrient intakes/day	Non-hypertensive	Hypertensive	p value
Energy (kcal)	1764.02±499.59	1821.40±489.13	0.473
Sodium (mg)	2230.63±794.54	2377.01±736.55	0.250
Vitamin E (mg)	8.5±3.2	8.8±5.6	0.318
Vitamin E with supplements (mg)	9.1±4.5	9.0±5.7	0.883
Serum α-Tocopherol (µmol/L)	20.0±5.6	20.5±5.6	0.652
Serum γ-Tocopherol (µmol/L)	1.2±0.5	1.1±0.5	0.134
Total Fat (g)	66.86±22.18	65.52±19.74	0.704
Saturated fatty acids (g)	24.72±0.89	24.81±0.30	0.989
Unsaturated fatty acids (g)	35.49±1.17	35.27±0.32	0.876
Cis monounsaturated fatty acids (g)	25.01±8.87	24.42±7.75	0.677
Cis n-3 fatty acids (g)	1.71±0.76	1.65±0.69	0.650
Cis n-6 fatty acids (g)	9.09±3.52	8.42±2.53	0.228
Trans fatty acids (g)	1.24±0.63	1.29±0.61	0.618
Low fat spread not polyunsaturated (g)	0.17±1.04	0.86±3.65	0.002*
Low fat spread polyunsaturated (g)	0.72±3.3	0.32±1.45	0.432
Reduced fat spread not polyunsaturated (g)	4.07±6.39	3.94±5.51	0.900
Reduced fat spread polyunsaturated (g)	1.11±3.84	0.7±2.5	0.496

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Other margarine fats and oils (g)	0.19±1.38	0.08±0.44	0.617
Total Fat percent total energy	33.87±4.75	32.45±5.38	0.065
Saturated fatty acids percent total energy	12.64±2.57	12.23±2.73	0.326
Cis monounsaturated fatty acids percent total energy	12.77±2.32	12.24±2.5	0.153
Cis n-3 fatty acids percent total energy	0.88±0.32	0.83±0.27	0.341
Cis n-6 fatty acids percent total energy	4.67±1.21	4.27±0.92	0.039*
Trans fatty acids percent total energy	0.63±0.25	0.63±0.23	0.956
Triglycerides (mmol/l)	0.84±0.42	0.96±0.43	0.131
Total cholesterol (mmol/l)	4.00±0.77	4.14±0.77	0.349
High density lipoproteins (mmol/l)	1.41±0.31	1.38±0.34	0.532
Low density lipoproteins (mmol/l)	2.25±0.65	2.38±0.67	0.331

* $P<0.05$ in t-tests

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2.4.4 Energy and nutrients intake and blood pressure Z scores (prelimimary analysis)

In the adjusted linear regression models, every 1mg increase in daily vitamin E intake was associated with 0.175 (95%CI: -0.330 to -0.020) lower SBPZ (p=0.027) (Table 2.4), and in logistic regression analysis, vitamin E intake (OR=0.065, 95%CI: 0.012 to 0.348, p=0.001) was found to be linked with a reduced risk of hypertension (Table 2.6).

In the adjusted linear regression models, every 1g increase in daily total fat intake was associated with 0.080 (95%CI: -0.142 to -0.019) lower DBPZ (p=0.011) (Table 2.5), and in logistic regression analysis, total fat intake (OR=0.638, 95%CI: 0.369 to 0.929, p=0.048) was found to be linked with a reduced risk of hypertension (Table 2.6).

In the adjusted linear regression models, every 1µg increase in daily vitamin A intake was associated with 0.074 (95%CI: -0.144 to -0.004) lower DBPZ (p=0.039) (Table 2.5). Every 1mg increase in daily niacin intake was associated with 0.072 (95%CI: -0.160 to -0.024) lower DBPZ (p=0.008) (Table 2.5). In logistic regression analysis, iodine intake (OR=1.496 95%CI: 1.107 to 2.024, p=0.009) was found to be linked with an increased risk of hypertension (Table 2.6).

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In the analysis of total fat and vitamin E, two significant associations were found between their daily intake and blood pressure levels, therefore, these two factors were included in further analysis. Due to the time limitation of the PhD programme, the factors that only found one significant association were not included.

Table 2.4 Change in systolic blood pressure Z-scores per unit of increased intake of energy and nutrients with supplements

Nutrient	Model 1				Model 2 †			
	Coefficient	95% CI		p Value	Coefficient	95% CI		p Value
Energy (kcal)	0.00001	-0.00002	0.00003	0.107	-0.00003	-0.00003	0.00003	0.860
Carbohydrate (g)	0.004	-0.074	0.082	0.914	0.047	-0.049	0.142	0.336
Total fat (g)	-0.044	-0.121	0.033	0.261	-0.027	-0.122	0.068	0.577
Protein (g)	0.030	-0.041	0.101	0.409	-0.007	-0.094	0.081	0.882
Sodium (mg)	0.079	0.007	0.152	0.031*	0.032	-0.051	0.115	0.446
Vitamin A (µg)	-0.362	-0.104	0.032	0.294	-0.664	-0.149	0.016	0.113
Thiamin (mg)	-0.012	-0.091	0.067	0.768	-0.060	-0.160	0.040	0.240
Riboflavin (mg)	-0.016	-0.091	0.060	0.685	-0.014	-0.099	0.071	0.745
Niacin (mg)	0.000	-0.072	0.072	0.997	-0.038	-0.118	0.042	0.350
VitaminB6 (mg)	-0.007	-0.075	0.061	0.837	-0.029	-0.102	0.043	0.428
VitaminB12 (µg)	-0.021	-0.089	0.046	0.533	-0.026	-0.104	0.051	0.502
Folate (µg)	-0.006	-0.080	0.067	0.868	-0.034	-0.125	0.057	0.466
Vitamin C (mg)	-0.020	-0.088	0.048	0.559	-0.024	-0.100	0.052	0.536
Vitamin D (µg)	-0.026	-0.102	0.050	0.499	-0.031	-0.115	0.054	0.479
Vitamin E (mg)	-0.192	-0.337	-0.047	0.010*	-0.175	-0.330	-0.020	0.027*
Iron (mg)	0.008	-0.033	0.048	0.717	0.011	-0.030	0.052	0.596
Calcium (mg)	0.039	-0.033	0.110	0.293	0.072	-0.013	0.155	0.095
Magnesium (mg)	-0.001	-0.076	0.073	0.971	-0.009	-0.101	0.083	0.846
Potassium (mg)	0.005	-0.067	0.078	0.889	0.011	-0.088	0.111	0.822
Zinc (mg)	0.017	-0.055	0.090	0.635	-0.029	-0.117	0.060	0.525
Copper (mg)	-0.073	-0.152	0.007	0.073	-0.079	-0.171	0.013	0.090
Selenium (µg)	0.011	-0.065	0.087	0.779	0.021	-0.067	0.109	0.633
Iodine (µg)	0.023	-0.046	0.092	0.516	0.042	-0.042	0.126	0.323

* $p<0.05$ in linear regression.

† Age, sex, smoking status, alcohol consumption, dietary energy intake, dietary sodium intake and social economic status were adjusted in all final models

Table 2.5 Change in diastolic blood pressure Z-scores per unit of increased intake of energy and nutrients with supplements

Nutrient	Model 1				Model 2 †			
	Coefficient	95% CI		p Value	Coefficient	95% CI		p Value
Energy (kcal)	-0.00001	-0.00002	0.00001	0.267	-0.00001	-0.00002	0.00002	0.953
Carbohydrate (g)	0.010	-0.057	0.077	0.770	0.059	-0.022	0.140	0.155
Fat (g)	-0.095	-0.152	-0.038	0.001*	-0.080	-0.142	-0.019	0.011*
Protein (g)	-0.040	-0.100	0.021	0.197	-0.031	-0.105	0.043	0.416
Sodium (mg)	0.003	-0.072	0.077	0.947	0.032	-0.051	0.115	0.446
Vitamin A (µg)	-0.063	-0.121	-0.006	0.032	-0.074	-0.144	-0.004	0.039*
Thiamin (mg)	-0.097	-0.164	-0.030	0.004*	-0.080	-0.165	0.005	0.065
Riboflavin (mg)	-0.063	-0.127	0.001	0.055	-0.055	-0.127	0.017	0.134
Niacin (mg)	-0.091	-0.152	-0.030	0.004*	-0.072	-0.160	-0.024	0.008*
VitaminB6 (mg)	0.010	-0.055	0.076	0.756	-0.034	-0.114	0.047	0.412
VitaminB12 (µg)	-0.028	-0.085	0.030	0.347	-0.039	-0.105	0.026	0.239
Folate (µg)	-0.086	-0.148	-0.024	0.007*	-0.071	-0.149	0.006	0.070
Vitamin C (mg)	-0.070	-0.127	-0.012	0.018*	-0.062	-0.127	0.002	0.058
Vitamin D (µg)	-0.059	-0.124	0.005	0.071	-0.054	-0.125	0.018	0.144
Vitamin E (mg)	-0.118	-0.242	0.006	0.061	-0.121	-0.253	0.012	0.074
Iron (mg)	-0.013	-0.048	0.022	0.465	-0.004	-0.039	0.030	0.808
Calcium (mg)	0.008	-0.053	0.070	0.791	0.029	-0.042	0.101	0.420
Magnesium (mg)	-0.069	-0.132	-0.006	0.032*	-0.023	-0.101	0.055	0.562
Potassium (mg)	-0.064	-0.126	-0.003	0.041*	-0.015	-0.100	0.069	0.719
Zinc (mg)	-0.044	-0.106	0.017	0.158	-0.033	-0.108	0.042	0.391
Copper (mg)	-0.005	-0.073	0.063	0.893	0.003	-0.075	0.081	0.940
Selenium (µg)	-0.037	-0.102	0.028	0.261	-0.041	-0.116	0.034	0.282
Iodine (µg)	-0.013	-0.072	0.046	0.674	-0.005	-0.076	0.067	0.902

* $p<0.05$ in linear regression.

† Age, sex, smoking status, alcohol consumption, dietary energy intake, dietary sodium intake and social economic status were adjusted in all final models

Table 2.6 Change in odds of having hypertension per unit of increased intake of energy and nutrients with supplements

Nutrient	Model 1				Model 2 †			
	OR	95% CI		p Value	OR	95% CI		p Value
Energy (kcal)	1.000	1.000	1.001	0.359	1.000	0.999	1.001	0.669
Carbohydrate (g)	1.392	0.977	1.984	0.068	1.522	0.949	2.442	0.082
Fat (g)	0.647	0.464	0.903	0.010*	0.638	0.396	0.929	0.048*
Protein (g)	1.049	0.774	1.422	0.756	1.078	0.734	1.583	0.703
Sodium (mg)	1.177	0.877	1.579	0.278	0.965	0.646	1.440	0.860
Vitamin A (µg)	0.719	0.453	1.140	0.160	0.666	0.360	1.234	0.197
Thiamin (mg)	1.002	0.711	1.413	0.991	1.019	0.623	1.669	0.939
Riboflavin (mg)	1.143	0.856	1.527	0.365	1.253	0.893	1.758	0.191
Niacin (mg)	0.939	0.666	1.322	0.718	0.870	0.551	1.375	0.551
VitaminB6 (mg)	0.857	0.571	1.286	0.455	0.818	0.491	1.364	0.441
VitaminB12 (µg)	1.041	0.788	1.375	0.776	1.196	0.893	1.603	0.230
Folate (µg)	0.982	0.710	1.360	0.915	0.957	0.613	1.493	0.846
Vitamin C (mg)	1.017	0.766	1.350	0.908	1.047	0.779	1.408	0.762
Vitamin D (µg)	0.803	0.546	1.182	0.267	0.914	0.585	1.428	0.692
Vitamin E (mg)	0.101	0.031	0.331	0.000*	0.065	0.012	0.348	0.001*
Iron (mg)	1.004	0.830	1.215	0.964	0.987	0.695	1.402	0.943
Calcium (mg)	1.168	0.878	1.553	0.287	1.411	0.996	1.998	0.052
Magnesium (mg)	0.926	0.659	1.300	0.656	0.899	0.567	1.425	0.649
Potassium (mg)	0.960	0.696	1.325	0.805	1.182	0.761	1.834	0.457
Zinc (mg)	1.076	0.802	1.443	0.625	1.045	0.695	1.570	0.834
Copper (mg)	0.793	0.541	1.163	0.235	0.619	0.363	1.055	0.078
Selenium (µg)	1.013	0.728	1.410	0.938	1.078	0.731	1.590	0.705
Iodine (µg)	1.262	0.999	1.595	0.051	1.496	1.107	2.024	0.009*

* $p<0.05$ in linear regression.

† Age, sex, smoking status, alcohol consumption, dietary energy intake, dietary sodium intake and social economic status were adjusted in all final models

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2.4.5 Dietary nutrients intake and serum tocopherols

No associations between dietary vitamin E intake (with or without supplements) and serum α- or γ- tocopherol were found (Table 2.7). Every 1g increase in daily cis n-3 fatty acids intake was associated with 0.090 (95%CI: -0.166 to -0.014) mmol/l lower serum total cholesterol (p=0.021), and with 0.080 (95%CI: -0.145 to -0.015) mmol/l lower serum LDL (p=-0.016). Every 1g increase in daily cis n-6 fatty acids intake was associated with 0.019 (95%CI: -0.036 to -0.002) mmol/l lower serum total cholesterol (p=0.027), and with 0.015 (95%CI: -0.030 to -0.001) mmol/l lower serum LDL (p=-0.040). See Table 2.8.

Table 2.7 Relationship between dietary vitamin E intake and serum tocopherols

Type of tocopherol	Increase in tocopherol for 1mg increase in vitamin E intakes	95%CI		p Value
Association with dietary vitamin E-diet only				
α- tocopherol (µmol/L)	-0.034	-0.147	0.080	0.558
γ- tocopherol (µmol/L)	0.003	-0.007	0.014	0.528
Association with dietary vitamin E-with supplements				
α- tocopherol (µmol/L)	-0.027	-0.104	0.050	0.496
γ- tocopherol (µmol/L)	0.005	-0.002	0.012	0.194

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Table 2.8 Association between dietary fat intake and serum lipid files

Type of dietary fats	Increase in serum lipid for 1g increase in fat intakes	95%CI		p Value
Association with total fat (g)				
Triglycerides (mmol/l)	0.001	-0.001	0.002	0.48
Total cholesterol (mmol/l)	-0.003	-0.005	0.000	0.061
High density lipoproteins (mmol/l)	-0.001	-0.002	0.000	0.214
Low density lipoproteins (mmol/l)	-0.002	-0.004	0.000	0.07
Association with Saturated fatty acids (g)				
Triglycerides (mmol/l)	0.000	-0.003	0.004	0.915
Total cholesterol (mmol/l)	-0.004	-0.011	0.002	0.176
High density lipoproteins (mmol/l)	-0.001	-0.003	0.002	0.515
Low density lipoproteins (mmol/l)	-0.004	-0.009	0.002	0.179
Association with cis monounsaturated fatty acids (g)				
Triglycerides (mmol/l)	0.002	-0.001	0.006	0.221
Total cholesterol (mmol/l)	-0.006	-0.013	0.001	0.07
High density lipoproteins (mmol/l)	-0.002	-0.005	0.001	0.111
Low density lipoproteins (mmol/l)	-0.005	-0.011	0.001	0.087

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Association with cis n-3 fatty acids (g)				
Triglycerides (mmol/l)	0.011	-0.032	0.053	0.618
Total cholesterol (mmol/l)	-0.090	-0.166	-0.014	0.021
High density lipoproteins (mmol/l)	-0.013	-0.044	0.019	0.434
Low density lipoproteins (mmol/l)	-0.080	-0.145	-0.015	0.016
Association with cis n-6 fatty acids (g)				
Triglycerides (mmol/l)	0.005	-0.005	0.014	0.325
Total cholesterol (mmol/l)	-0.019	-0.036	-0.002	0.027
High density lipoproteins (mmol/l)	-0.006	-0.013	0.001	0.091
Low density lipoproteins (mmol/l)	-0.015	-0.030	-0.001	0.040*
Association with trans fatty acids (g)				
Triglycerides (mmol/l)	-0.010	-0.065	0.046	0.738
Total cholesterol (mmol/l)	-0.012	-0.114	0.089	0.809
High density lipoproteins (mmol/l)	0.016	-0.026	0.057	0.464
Low density lipoproteins (mmol/l)	-0.018	-0.105	0.069	0.684

* $p<0.05$ in univariable linear regression.

2.4.6 Associations between dietary vitamin E, serum tocopherols and blood pressure

In the adjusted linear regression analysis, every 1mg increase in daily vitamin E intake (with supplements) was associated with 0.234 (95%CI: -0.427 to -0.034) mmHg lower SBP (p=0.022), and was associated with 0.019 (95%CI: -0.038 to -0.001) lower SBPZ (p=0.042). However, no statistically significant relationship was found between vitamin E status and DBP of DBPZ (See Table 2.9). In logistic regression analysis, supplements including vitamin E intake (OR=0.879, 95%CI: 0.776 to 0.995, p=0.042) was found to be linked with reduce risk of hypertension. No statistically significant effect of serum tocopherols on the risk of hypertension were found in the studied population (See Table 2.10).

Table 2.9 Association between dietary vitamin E, serum tocopherols and blood pressure levels

Nutrients	Change in BP per unit change in exposure							
	Non-adjusted models				Fully-adjusted models †			
	Coefficient	95%CI		P value	Coefficient	95%CI		P value
With systolic blood pressure								
Vitamin E with supplements (mg)	0.169	0.040	0.297	0.010*	-0.231	-0.427	-0.034	0.022*
Vitamin E diet only (mg)	0.378	0.205	0.551	<0.001*	-0.195	-0.495	0.105	0.202
Serum α-tocopherol (μmol/L)	0.038	-0.114	0.189	0.625	0.063	-0.133	0.259	0.528
Serum γ-tocopherol (μmol/L)	-0.034	-1.754	1.687	0.969	-0.480	-2.817	1.858	0.687
With diastolic blood pressure								
Vitamin E with supplements (mg)	-0.005	-0.109	0.098	0.917	-0.053	-0.232	0.126	0.560
Vitamin E diet only (mg)	-0.034	-0.174	0.106	0.635	-0.056	-0.328	0.216	0.684
Serum α-tocopherol (μmol/L)	0.084	-0.035	0.203	0.168	0.051	-0.118	0.220	0.555
Serum γ-tocopherol (μmol/L)	0.883	-0.470	2.237	0.200	0.578	-1.434	2.591	0.572
With systolic blood pressure Z-scores								
Vitamin E with supplements (mg)	-0.001	-0.014	0.011	0.814	-0.019	-0.038	-0.001	0.042*
Vitamin E diet only (mg)	0.008	-0.008	0.023	0.338	-0.013	-0.042	0.016	0.378
Serum α-tocopherol (μmol/L)	0.010	-0.005	0.024	0.194	0.004	-0.015	0.024	0.665
Serum γ-tocopherol (μmol/L)	-0.020	-0.175	0.135	0.801	-0.080	-0.310	0.150	0.495
With diastolic blood pressure Z-scores								
Vitamin E with supplements (mg)	-0.009	-0.020	0.001	0.090	-0.005	-0.021	0.011	0.515
Vitamin E diet only (mg)	-0.011	-0.025	0.002	0.097	-0.003	-0.028	0.021	0.788
Serum α-tocopherol (μmol/L)	0.010	-0.003	0.022	0.124	0.004	-0.011	0.020	0.600
Serum γ-tocopherol (μmol/L)	0.077	-0.053	0.208	0.246	0.024	-0.160	0.208	0.798

* $p<0.05$ in multiple linear regression. † Age, sex, energy intake excluding fats, sodium intake, height, BMI category, smoking, alcohol intake, SES, ethnicity were adjusted in all final models.

Table 2.10 Association between dietary vitamin E, serum tocopherols and prevalence of hypertension

Nutrients	Non-adjusted models				Fully-adjusted models †			
	OR	95%CI		p Value	OR	95%CI		p Value
Vitamin E with supplements (mg)	0.998	0.950	1.049	0.942	0.879	0.776	0.995	0.042*
Vitamin E diet only (mg)	1.029	0.970	1.091	0.341	0.898	0.779	1.036	0.139
Serum α-Tocopherol (μmol/L)	1.014	0.952	1.081	0.659	0.986	0.894	1.089	0.786
Serum γ-Tocopherol (μmol/L)	0.651	0.278	1.525	0.323	0.391	0.115	1.325	0.132

*$p<0.05$ in logistic regression

† Age, sex, energy intake excluding fats, sodium intake, height, BMI category, smoking, alcohol intake, SES, ethnicity were adjusted in all final models.

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2.4.7 Associations between dietary fats intake, serum lipids and blood pressure

In the fully adjusted linear regression analysis, every 1g increase in daily trans fatty acids intake was associated with 1.472 (95%CI: 0.068 to 2.867) mmHg higher SBP (p=0.040), and was associated with 0.134 (95%CI: 0.0001 to 0.272) lower SBPZ (p=0.047), see Table 2.11. No statistically significant effect of dietary fat percent total energy on blood pressure levels were found in the studied population (Table 2.12). Every 1g increase in daily polyunsaturated low fat spread intake was associated with 0.858 (95%CI: -1.601 to -0.115) mmHg higher SBP (p=0.047), see Table 2.13.
In the fully adjusted linear regression analysis, every 1mmol/g increase in serum total cholesterol was associated with 0.013 (95%CI: 0.002 to 0.024) mmHg higher SBP (p=0.026), and was associated with 0.131 (95%CI: 0.005 to 0.258) higher SBPZ (p=0.042), see Table 2.14. No statistically significant association between dietary fats intake, serum lipid profile and the prevalence of hypertension was found in the studied population (Table 2.15).

Table 2.11 Association between dietary fat intake and blood pressure

Nutrients	Change in BP per unit change in exposure							
	Non-adjusted models				Fully-adjusted models †			
	Coefficient	95%CI		P value	Coefficient	95%CI		P value
With systolic blood pressure								
Total Fat (g)	0.049	-0.105	0.203	0.533	-0.073	-0.491	0.345	0.731
Saturated fatty acids(g)	0.206	-0.159	0.571	0.269	0.488	-0.283	1.258	0.214
Cis monounsaturated fatty acids (g)	0.088	-0.299	0.476	0.656	-0.446	-1.309	0.416	0.310
Cis n-3 fatty acids (g)	-2.396	-6.628	1.836	0.267	-5.434	-11.256	0.387	0.067
Cis n-6 fatty acids (g)	-0.214	-1.187	0.759	0.666	-1.456	-3.018	0.105	0.067
Trans fatty acids (g)	4.563	-1.030	10.156	0.110	1.472	0.068	2.867	0.040*
With diastolic blood pressure								
Total Fat (g)	0.005	-0.084	0.094	0.913	-0.042	-0.284	0.200	0.733
Saturated fatty acids(g)	0.070	-0.140	0.280	0.512	0.248	-0.198	0.693	0.276
Cis monounsaturated fatty acids (g)	-0.001	-0.223	0.222	0.995	-0.211	-0.710	0.288	0.407
Cis n-3 fatty acids (g)	-2.136	-4.566	0.294	0.085	-3.488	-6.855	0.121	0.142
Cis n-6 fatty acids (g)	-0.248	-0.807	0.311	0.385	-0.783	-1.687	0.121	0.089
Trans fatty acids (g)	1.913	-1.303	5.129	0.243	3.548	-0.999	8.095	0.126
With systolic blood pressure Z-scores								
Total Fat (g)	0.001	-0.002	0.005	0.406	-0.003	-0.011	0.005	0.471
Saturated fatty acids(g)	0.004	-0.004	0.012	0.371	-0.004	-0.019	0.011	0.587
Cis monounsaturated fatty acids (g)	0.003	-0.005	0.012	0.428	-0.003	-0.019	0.014	0.742
Cis n-3 fatty acids (g)	-0.018	-0.115	0.079	0.716	-0.072	-0.196	0.052	0.255
Cis n-6 fatty acids (g)	0.002	-0.019	0.023	0.847	-0.010	-0.041	0.021	0.523
Trans fatty acids (g)	0.089	-0.028	0.207	0.136	0.134	0.0001	0.272	0.047*
With diastolic blood pressure Z-scores								

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Total Fat (g)	-0.002	-0.005	0.001	0.263	-0.002	-0.011	0.006	0.589
Saturated fatty acids(g)	-0.003	-0.009	0.004	0.439	-0.007	-0.022	0.008	0.364
Cis monounsaturated fatty acids (g)	-0.003	-0.011	0.004	0.360	0.005	-0.011	0.022	0.517
Cis n-3 fatty acids (g)	-0.123	-0.205	-0.040	0.004*	-0.107	-0.227	0.013	0.079
Cis n-6 fatty acids (g)	-0.013	-0.031	0.005	0.154	-0.008	-0.038	0.022	0.616
Trans fatty acids (g)	-0.028	-0.129	0.073	0.587	0.028	-0.118	0.174	0.708

* $p<0.05$ in multiple linear regression.

† Age, sex, energy intake excluding fats, sodium intake, height, BMI category, smoking, alcohol intake, SES and ethnicity were adjusted in all final models.

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Table 2.12 Association between dietary fat percent total energy and blood pressure (n=580)

Nutrients	Change in BP per unit change in exposure							
	Non-adjusted models				Fully-adjusted models †			
	Coefficient	95%CI		P value	Coefficient	95%CI		P value
With systolic blood pressure								
Total fat percent total energy	-0.003	-0.695	0.689	0.994	-0.178	-0.986	0.631	0.666
Saturated fatty acids percent total energy	0.729	-0.580	2.038	0.275	0.854	-0.674	2.382	0.273
Cis monounsaturated fatty acids percent total energy	-0.240	-1.663	1.182	0.741	-0.928	-2.592	0.737	0.274
Cis n-3 fatty acids percent total energy	-9.384	-19.540	0.773	0.070	-9.608	-21.033	1.817	0.099
Cis n-6 fatty acids percent total energy	-1.960	-4.764	0.843	0.170	-2.623	-5.756	0.511	0.101
Trans fatty acids percent total energy	9.222	-4.988	23.432	0.203	11.607	-3.962	27.176	0.144
With diastolic blood pressure								
Total fat percent total energy	0.034	-0.364	0.432	0.868	-0.092	-0.560	0.376	0.700
Saturated fatty acids percent total energy	0.469	-0.284	1.221	0.222	0.452	-0.433	1.336	0.316
Cis monounsaturated fatty acids percent total energy	-0.048	-0.865	0.770	0.909	-0.435	-1.398	0.529	0.376
Cis n-3 fatty acids percent total energy	-6.073	-11.907	-0.238	0.041	-6.194	-12.801	0.413	0.066
Cis n-6 fatty acids percent total energy	-1.070	-2.681	0.542	0.193	-1.421	-3.235	0.392	0.124
Trans fatty acids percent total energy	4.865	-3.302	13.033	0.243	6.338	-2.671	15.347	0.168

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With systolic blood pressure Z-scores								
Total fat percent total energy	-0.006	-0.021	0.010	0.468	-0.001	-0.017	0.015	0.876
Saturated fatty acids percent total energy	-0.002	-0.031	0.026	0.885	-0.004	-0.037	0.027	0.766
Cis monounsaturated fatty acids percent total energy	-0.010	-0.041	0.021	0.533	0.016	-0.016	0.049	0.321
Cis n-3 fatty acids percent total energy	-0.221	-0.456	0.015	0.066	-0.203	-0.436	0.029	0.086
Cis n-6 fatty acids percent total energy	-0.030	-0.091	0.032	0.342	-0.010	-0.071	0.050	0.745
Trans fatty acids percent total energy	0.166	-0.135	0.468	0.279	0.057	-0.233	0.347	0.700
With diastolic blood pressure Z-scores								
Total fat percent total energy	0.003	-0.010	0.017	0.621	-0.005	-0.021	0.011	0.511
Saturated fatty acids percent total energy	0.009	-0.015	0.034	0.458	-0.007	-0.036	0.022	0.649
Cis monounsaturated fatty acids percent total energy	0.009	-0.018	0.036	0.498	-0.005	-0.037	0.027	0.766
Cis n-3 fatty acids percent total energy	-0.264	-0.466	-0.063	0.010*	-0.163	-0.402	0.075	0.179
Cis n-6 fatty acids percent total energy	-0.010	-0.063	0.043	0.716	-0.019	-0.080	0.043	0.546
Trans fatty acids percent total energy	0.039	-0.221	0.299	0.77	0.133	-0.163	0.429	0.377

* $p<0.05$ in multiple linear regression.

† Age, sex, energy intake excluding fats, sodium intake, height, BMI category, smoking, alcohol intake, SES, ethnicity were adjusted in all final models.

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Table 2.13 Association between dietary margarine fats/oil intakes and blood pressure

Nutrients	Change in BP per unit change in exposure							
	Non-adjusted models				Fully-adjusted models †			
	Coefficient	95%CI		P value	Coefficient	95%CI		P value
With systolic blood pressure								
Low fat spread not polyunsaturated (g)	-0.761	-2.939	1.416	0.493	0.045	-2.295	2.385	0.970
Low fat spread polyunsaturated (g)	-0.498	-1.539	0.543	0.348	-1.281	-2.566	0.004	0.051
Reduced fat spread not polyunsaturated(g)	0.130	-0.434	0.694	0.651	-0.074	-0.689	0.542	0.814
Reduced fat spread polyunsaturated (g)	-0.297	-1.212	0.618	0.524	-0.409	-1.415	0.598	0.426
Other margarine fats and oils (g)	2.444	-0.791	5.679	0.138	-1.281	-2.566	0.004	0.051
With diastolic blood pressure								
Low fat spread not polyunsaturated (g)	-0.387	-1.638	0.865	0.545	0.174	-1.179	1.528	0.801
Low fat spread polyunsaturated (g)	-0.386	-0.984	0.212	0.206	-0.858	-1.601	-0.115	0.047*
Reduced fat spread not polyunsaturated(g)	0.078	-0.246	0.402	0.636	-0.039	-0.395	0.317	0.830
Reduced fat spread polyunsaturated (g)	-0.192	-0.718	0.334	0.474	-0.204	-0.786	0.379	0.492
Other margarine fats and oils (g)	1.287	-0.573	3.146	0.175	0.441	-1.928	2.810	0.715

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With systolic blood pressure Z-scores								
Low fat spread not polyunsaturated (g)	-0.002	-0.071	0.068	0.965	0.003	-0.065	0.070	0.940
Low fat spread polyunsaturated (g)	0.003	-0.020	0.026	0.788	0.002	-0.020	0.025	0.843
Reduced fat spread not polyunsaturated(g)	0.011	0.000	0.023	0.060	0.008	-0.004	0.019	0.187
Reduced fat spread polyunsaturated (g)	0.006	-0.013	0.026	0.524	0.007	-0.012	0.026	0.459
Other margarine fats and oils (g)	-0.006	-0.061	0.049	0.832	-0.008	-0.062	0.046	0.771
With diastolic blood pressure Z-scores								
Low fat spread not polyunsaturated (g)	-0.001	-0.061	0.058	0.969	0.023	-0.047	0.093	0.517
Low fat spread polyunsaturated (g)	-0.010	-0.030	0.010	0.321	-0.015	-0.054	0.0001	0.063
Reduced fat spread not polyunsaturated(g)	0.008	-0.002	0.018	0.135	0.008	-0.003	0.020	0.147
Reduced fat spread polyunsaturated (g)	-0.002	-0.019	0.015	0.841	0.005	-0.015	0.024	0.628
Other margarine fats and oils (g)	-0.015	-0.062	0.033	0.545	-0.016	-0.079	0.048	0.625

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* $p<0.05$ in multiple linear regression.

† Age, sex, energy intake excluding fats, sodium intake, height, BMI category, smoking, alcohol intake, SES, ethnicity were adjusted in all final models.

Table 2.14 Association between serum lipid profile and blood pressure

Lipid profile factors	Change in BP per unit change in exposure							
	Non-adjusted models				Fully-adjusted models †			
	Coefficient	95%CI		P value	Coefficient	95%CI		P value
With systolic blood pressure								
Triglycerides (mmol/l)	0.006	0.003	0.009	<0.001*	0.005	0.000	0.011	0.072
Total cholesterol (mmol/l)	-0.002	-0.008	0.003	0.407	0.004	-0.006	0.014	0.393
High density lipoproteins (mmol/l)	-0.006	-0.008	-0.003	<0.001*	-0.002	-0.006	0.002	0.285
Low density lipoproteins (mmol/l)	0.000	-0.004	0.005	0.857	0.004	-0.005	0.012	0.405
With diastolic blood pressure								
Triglycerides (mmol/l)	0.006	0.002	0.010	0.003*	0.005	-0.002	0.011	0.152
Total cholesterol (mmol/l)	0.011	0.004	0.019	0.001*	0.013	0.002	0.024	0.026*
High density lipoproteins (mmol/l)	-0.001	-0.004	0.002	0.502	0.001	-0.003	0.006	0.526
Low density lipoproteins (mmol/l)	0.010	0.004	0.016	0.002*	0.009	-0.001	0.018	0.087

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With systolic blood pressure Z-scores								
Triglycerides (mmol/l)	0.048	0.010	0.086	0.013*	0.059	-0.002	0.120	0.057
Total cholesterol (mmol/l)	0.044	-0.025	0.113	0.211	0.072	-0.035	0.178	0.187
High density lipoproteins (mmol/l)	-0.024	-0.052	0.004	0.096	-0.012	-0.053	0.029	0.568
Low density lipoproteins (mmol/l)	0.046	-0.013	0.105	0.124	0.052	-0.040	0.144	0.271
With diastolic blood pressure Z-scores								
Triglycerides (mmol/l)	0.043	0.000	0.086	0.053	0.052	-0.021	0.125	0.160
Total cholesterol (mmol/l)	0.145	0.068	0.223	<0.001*	0.131	0.005	0.258	0.042*
High density lipoproteins (mmol/l)	0.011	-0.021	0.043	0.519	0.010	-0.039	0.058	0.701
Low density lipoproteins (mmol/l)	0.115	0.048	0.181	0.001*	0.089	-0.021	0.199	0.111

* $p<0.05$ in multiple linear regression.

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† Age, sex, energy intake excluding fats, sodium intake, height, BMI category, smoking, alcohol intake, SES, ethnicity were adjusted in all final models.

Table 2.15 Association between dietary fat intake, serum lipid and prevalence of hypertension

Nutrients	Non-adjusted models				Fully-adjusted models†			
	OR	95%CI		p value	OR	95%CI		p value
Total Fat (g)	1.00	0.98	1.01	0.703	0.98	0.96	1.01	0.124
Saturated fatty acids(g)	1.00	0.97	1.03	0.989	0.96	0.90	1.04	0.317
Unsaturated fatty acid (g)					0.97	0.94	1.02	0.225
Cis monounsaturated fatty acids (g)	0.99	0.96	1.03	0.676	0.93	0.86	1.02	0.110
Cis n-3 fatty acids (g)	0.90	0.59	1.40	0.650	0.89	0.47	1.70	0.723
Cis n-6 fatty acids (g)	0.94	0.85	1.04	0.227	0.86	0.73	1.03	0.103
Trans fatty acids (g)	1.13	0.70	1.83	0.618	0.94	0.47	1.88	0.870
Total Fat percent total energy	0.94	0.88	1.00	0.065	0.94	0.87	1.02	0.115
Saturated fatty acids percent total energy	0.94	0.83	1.06	0.326	0.92	0.79	1.07	0.265
Cis monounsaturated fatty acids percent total energy	0.91	0.80	1.05	0.190	0.92	0.78	1.08	0.300
Cis n-3 fatty acids percent total energy	0.58	0.19	1.80	0.346	0.90	0.25	3.22	0.869
Cis n-6 fatty acids percent total energy	0.74	0.55	1.00	0.050	0.82	0.58	1.14	0.236
Trans fatty acids percent total energy	1.03	0.29	3.74	0.959	0.85	0.21	3.46	0.823
Low fat spread not polyunsaturated (g)	1.18	1.02	1.36	0.022	1.14	0.90	1.45	0.266
Low fat spread polyunsaturated (g)	0.93	0.77	1.12	0.441	0.92	0.75	1.13	0.434
Reduced fat spread not polyunsaturated (g)	0.96	0.86	1.08	0.500	1.00	0.95	1.05	0.955

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Reduced fat spread polyunsaturated (g)	1.00	0.95	1.05	0.899	0.97	0.86	1.10	0.680
Other margarine fats and oils (g)	0.89	0.56	1.43	0.637	0.93	0.61	1.41	0.741
Triglycerides (mmol/l)	1.70	0.85	3.43	0.134	3.09	0.88	10.84	0.079
Total cholesterol (mmol/l)	1.25	0.79	1.97	0.349	0.95	0.44	2.05	0.888
High density lipoproteins (mmol/l)	0.68	0.20	2.29	0.531	0.49	0.07	3.56	0.485
Low density lipoproteins (mmol/l)	1.31	0.76	2.24	0.330	0.84	0.34	2.07	0.701

* $p<0.05$ in logistic regression

† Age, sex, energy intake excluding fats, sodium intake, height, BMI category, smoking, alcohol intake, SES, ethnicity were adjusted in all final models.

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2.5 Discussion

2.5.1 Summary of the results

This study is the first to determine the associations between vitamin E intake, serum tocopherol, dietary fats intake, serum lipids profile and blood pressure in the UK adolescents using cross-sectional representative national data. Mean SBP was 111.3±11.1 mmHg, and mean DBP was 62.8±8.9 mmHg. Seven percent of the total sample were defined as hypertensive. Both daily cis n-3 fatty acids and cis n-6 fatty acids were associated with lower serum total cholesterol and lower serum LDL.

Higher intakes of vitamin E including supplements intake were associated with lower SBP and SBPZ, and were associated with lower risk of hypertension. Higher dietary trans fatty acids was linked with higher SBP and higher SBPZ. Higher dietary polyunsaturated low fat spread intake was linked with higher SBP. Higher serum total cholesterol was associated with higher SBP and SBPZ.

2.5.2 Prevalence of hypertension in UK adolescents

During the studied years (2008 to 2012), there was no significant increasing trend in the prevalence of hypertension in adolescents. However, the overall prevalence of hypertension estimated in NDNS adolescent population was similar to other studies in US and Europe, where prevalence of hypertension is reported to be between 4.5% and 8.2% (Martin et al., 2015, Sorof et al., 2004). A cross-sectional study in the US estimated the prevalence of elevated blood pressure in 10 to 19 year old adolescents to be 4.5%, however some of the adolescents defined as hypertensive in the first screening dropped out during the following two screenings, therefore, the prevalence could have been underestimated (Sorof et al., 2004). Although the prevalence of hypertension in adolescents is much lower than that in adults, a number of studies suggest that elevated blood pressure in youth is a strong predictor of adulthood hypertension (Sun et al., 2007, Chen and Wang, 2008). Even children and adolescents with normal blood pressure levels in the higher range of the blood pressure distribution are at higher risk of developing into hypertensive adults. In a longitudinal study (Tirosh et al., 2010), 17 year old adolescents with high normal blood pressure values at 130 to 139/85 to 89 mm Hg were found to have more than double the risk of developing into hypertensive adults between ages 17 and 42 years, the hazard ratio was 2.50 (95%CI: 1.75 to 3.57) for boys and 2.31(95%CI: 0.71 to 7.60) for girls.

2.5.3 Previous studies and mechanism

The mean intake of dietary vitamin E ranged from 7 to 9 mg/d, which is higher than the reference intake of UK (Institute of Medicine. Standing Committee on the Scientific Evaluation of Dietary Reference et al., 2003). We found that higher vitamin E intakes were associated with decreased risk of hypertension. Several previous epidemiological studies in adults and children, but not adolescents support the results (Mishra et al., 2003, Boshtam et al., 2002). A randomized controlled clinical trial found that vitamin E supplements could reduce both SBP and DBP in mild hypertensive adult patients (Boshtam et al., 2002). A longitudinal study (1950-1989) in the UK found that vitamin E intake from foods in both childhood and adulthood can predict hypertension in adulthood (Mishra et al., 2003). The participants were recruited at 4 years old and then followed up 40 years later. 24-hour and 48-hour dietary recalls were used respectively at these two time points. It was a long term study, which collected data in childhood and in middle age, however the method used for assessing diet may have caused recall bias, and no data in adolescence was obtained.

Experimental studies can clarify the mechanism of the protective effect of vitamin E on hypertension. One possible mechanism is that serum vitamin E reduces oxidant stress (Rodrigo et al., 2008, Lobo et al., 2008, Jiang, 2014). It can function as a chain-breaking antioxidant, reacting with key factors that induce peroxidation, for example tert-Butyl hydroperoxide (tBuOOH) (Brigelius-Flohe and Traber, 1999, Ham and Liebler, 1997). In that way, tocopherol can protect serum LDL against oxidation (Lobo et al., 2008). As ox-LDL formation is found to be related to the progression of hypertension (Silva et al., 2013), serum tocopherol may reduce the risk of hypertension by that route. Another possible mechanism may be that vitamin E could reduce inflammatory response by inhibiting the activity of PGE2 and LTB4 (Reiter et al., 2007, Rodrigo et al., 2008, Kromhout, 2001, Jiang, 2014), which is believed to be associated with cardiovascular disease (Aeberli et al., 2006).

In the current study, significant association was found between dietary vitamin E intake and SBP, but not DBP. SBP, an indicator of stiffness of large arteries, is given more attention as a better predictor of cardiovascular disease and mortality in adults, especially in elderly people (Strandberg and Pitkala, 2003). In children and adolescents, arterial stiffness was also considered to be linked with increased SBP variability (Stabouli et al., 2015). The mechanism could be the antioxidant ability of vitamin E

which improves the endothelial function and arterial stiffness (Plantinga et al., 2007, Park et al., 2016).

In children and adolescents, both observational studies and randomized controlled trial were found exploring the relationship between dietary fats intake and blood pressure. However the results remain conflict. Total fat (Aeberli et al., 2009, Mirza et al., 2013, Setayeshgar et al., 2017b), MUFA (Aeberli et al., 2009, Sugiyama et al., 2007) and total cholesterol (Ventura et al., 2008) intake were found to be linked with increased blood pressure, while SFA (Aeberli et al., 2009, Post et al., 1997) intake was found to be linked with decreased blood pressure. Results of the current study may add evidence to this area.

Trans fatty acids was found to increase LDL concentrations, and do not increase HDL concentrations. These differences may have been attributed to higher CVD risk (Lichtenstein, 2014), and could be the mechanism to increase systolic blood pressure and systolic blood pressure Z-scores. The potential mechanism of PUFA's effect to lower blood pressure might be its anti-inflammatory function (McDougle et al., 2017).

Higher intake of low fat polyunsaturated spread was found to be linked with lower diastolic blood pressure in adolescents. Higher intake of low fat polyunsaturated spread indicated a relevant lower intake of other kind of fat spread, for example whole fat spread, leading to a lower intake of total and saturated fatty acids. Lower total fat intake and higher polyunsaturated intake was found to be linked with lower blood pressure levels in adults (Ruparelia et al., 2017, Sverdlov et al., 2016, Longhi et al., 2018, Munoz and Costa, 2013, Wang et al., 2012, de Roos et al., 2009) and adolescents (Aeberli et al., 2009, Mirza et al., 2013, Setayeshgar et al., 2017b). This could be the potential reason for the relationship.

A higher concentrate of serum cholesterol was found to be associated with higher DBP and DBPZ in NDNS adolescents. The result agreed with previous studies both in adolescents (Ventura et al., 2008) and adults (Orozco-Beltran et al., 2017, Lewington et al., 2007). Total serum cholesterol consists largely of the cholesterol in low-density lipoprotein particles (LDL) and the cholesterol in high-density lipoprotein particles (HDL), which have opposite associations with blood pressure. LDL was found to be associated with higher blood pressure and higher risk of cardiovascular disease such as stroke (Baigent et al., 2005), while HDL was found to have preventive effects (Turak et

al., 2016). However, metabolic interactions between lipoprotein particles are complex, lowering a particular lipid variable does not necessarily equate with utility in risk prediction. Studies indicated that LDL alone provided less information about chronic heart disease risk than total cholesterol (Barzi et al., 2005).

2.5.4 Selecting of confounders

The confounders that were adjusted in each final model were determined using a DAG (Figure 2.1) and also referring to the confounders adjusted in previous relevant studies. Age, gender, BMI, height and ethnicity were included as confounders in the major of previous studies, therefore they were included in this analysis. Physical activity is linked with both blood pressure levels and diet, but it was not adjusted in the final models, as it is in the same route with BMI and energy intake. Adjusting for all these three factors may cause over adjusting. Considering physical activity data was obtained using different methods by research year and the age of participants, it will lose information if a combined physical activity variable is generated. While the method of collecting energy intake data and BMI data is more consistent, we decided to include energy and BMI rather than physical activity in the final models.

Both height and BMI were included in the final models. Although height is a component of BMI, including both of them could cause bias by over adjusting (Keevil and Khaw, 2014). BMI and height are both independently associated with blood pressure. In adolescents aged 10 to 19 years, their height should be regarded as an index of body growth, development and puberty, which ranges widely in this age group (Bahchachi et al., 2016). Height could have a greater influence on blood pressure in adolescents than in adults. Therefore, both BMI and height were included in the final models.

Metal stress is a potential confounder in the relationship between diet and blood pressure levels, but it was not included in the final models as this information was not collected in the NDNS.

Bias may appear for the above reasons. Therefore, it should be cautiously applied when generalizing the results to a broader population.

2.5.5 Strengths and Limitations

The National Diet and Nutrition Survey (NDNS) is a large national nutrition survey in the UK, in which a representative sample of UK population is selected, and high quality data is collected. Blood pressure was measured and blood samples were collected by trained nurses using standard protocols. No previous publication of diet and blood pressure in adolescents using NDNS was found.

The main limitation of the study is that it is a cross-sectional study, and therefore is not able to provide causal relationships. However, there are few trials or prospective studies in this age group. In the analysis, some of the samples were excluded from the analysis due to missing data, particularly on blood pressure. These figures might therefore not be representative of the total sample or the population of British adolescents and may have introduced bias into the results. Dietary data was derived over a relatively short period of 4 days which may be insufficient to measure micronutrients such as variation in dietary vitamin E. Indeed there was little association between dietary vitamin E and alpha-tocopherol. Positive relationships between vitamin E intake and serum tocopherols were found in previous studies, where a food frequency questionnaire was used to measure long term diet for at least 3 months (Sauvageot et al., 2013, Galan et al., 2005)). Nevertheless, in the NDNS pilot study, dietary records were found to have acceptable response rates and was adaptable for a large population, especially for children and adolescents (Public-Health-England and Food-Standards-Agency, 2014). Family history of hypertension is known to affect blood pressure (Westerdahl et al., 2013); however this data was not available to include in the analysis.

2.5.6 Perspective

Nuts are high in vitamin E and fats, and previous studies have reported that nuts might affect blood pressure (Aeberli et al., 2009, O'Neil et al., 2012). A cross-sectional study found that nut consumption was associated with a lower risk of hypertension in adults but not in adolescents (O'Neil et al., 2012).The relationships between nuts intake and blood pressure in adolescents are not clear and need to be explored.

Results from the current study may provide evidence and clues for studies exploring diet and blood pressure in adolescents, but should be carefully generalized to a broader age range and to other populations. The conclusions should be confirmed by further

studies of stronger study design such as prospective cohorts, randomised controlled trials or epigenetic studies.

2.6 Conclusion

In the 10 to 19 year old National Diet and Nutrition Survey 2008-2014 population,

1. The prevalence of hypertension was 7%
2. Higher dietary vitamin E intake was found to have associations with lower systolic blood pressure, lower systolic blood pressure Z-scores and lower risk of hypertension.
3. Higher dietary trans fatty acids was linked with higher SBP and higher SBPZ. Higher dietary polyunsaturated low fat spread intake was linked with higher SBP. Higher serum total cholesterol was associated with higher SBP and SBPZ.

Chapter 3. Dietary vitamin E, fat intake and blood pressure level in UK adolescents: a longitudinal analysis

Abstract

Background: Previous studies supported that dietary vitamin E and fats intake was associated with blood pressure levels, however their results were conflicting. Relevant studies in adolescents are lacking, especially longitudinal studies. The aim of this study is to determine the longitudinal relationship between dietary vitamin E intake, dietary fats intake and blood pressure in UK adolescents.

Methods: A sample of participants was selected from the Avon Longitudinal Study of Parents and Children (ALSPAC), in which sample was drawn randomly. General information and blood pressure data were collected at age 10, 11, 12, 13, 15 and 17. Diet was assessed using a four-day food record at age 10 and 13. Blood pressure data was transformed to systolic/diastolic blood pressure Z-scores (SBPZ/DBPZ). Multivariable linear regression was undertaken to explorer the relationships between vitamin E, fat intake and future blood pressure levels. Participants were grouped into low/medium/high vitamin E or fat intake group according to their total fat intake. Incidence rate and mean survival time was calculated in each group. Cox regression was used to explore the longitudinal relationship. Gender, ethnicity, BMI, alcohol intake, smoking status, sodium intake, energy intake excluding fat, parents' hypertension history and household income were adjusted in each model.

Results and Conclusion: In the ALSPAC population, prevalence of hypertension was approximately 10% as they were adolescents. Higher dietary vitamin E intake was found to have longitudinal associations with increased later DBP, DBPZ, SBPZ and risk of hypertension. Higher dietary total fat intake at was found to have longitudinal associations with increased later SBP, SBPZ and risk of hypertension. Except when blood pressure level at age 15 is considered as an outcome, higher vitamin E and total fat intakes were found to be linked with lower SBP and/or lower risk of hypertension at that age.

3.1 Introduction

3.1.1 Brief description of data

The Avon Longitudinal Study of Parents and Children (ALSPAC) is a prospective observational study exploring the factors that may affect health and development across the life course (Boyd et al., 2013).

In the year of 1985, WHO Europe sponsored a meeting in Moscow recommending that birth cohorts should be established across Europe to investigate the influences on children's development and health. The European Longitudinal Study of Pregnancy and Childhood was then initiated in seven independent centres including Bristol in the UK, Isle of Man, the Czech Republic, Slovakia, Ukraine, Greece and Russia (Piler et al., 2017). ALSPAC was one of those cohorts. During 1990 to 1992, all pregnant women in the Bristol area received invitation from the research team, and 14541 of them were actually enrolled, which consisted of the initial sample. The mothers, their partners, their children born during that time period and the next generation of those children have been followed up until now, as the initial sample enlarged while some of the participants were excluded or dropped out. Follow-up includes postal questionnaires and clinical assessment visits. A diverse range of information that related to health was collected, such as social economic status, anthropometric measures, dietary data, developmental outcomes and genetic information. Biological samples were collected at several follow-up sessions.

Detailed methods related to the analysis of sampling and data collection will be described in the Method section of this Chapter.

3.1.2 Existing literature on dietary intake of vitamin E, fat and blood pressure in adolescents

The influence of dietary vitamin E intake on blood pressure had been reported in several adult epidemiologic studies, but the results are inconsistent (Boshtam et al., 2002, Llopis-Gonzalez et al., 2015, Kuwabara et al., 2014). The influence of dietary fat intake was explored in adult, most of the studies suggest higher fat intake could be associated with higher blood pressure values (Schwingshackl et al., 2011, Schwab et al., 2014, Appel et al., 1997, Boden-Albala et al., 2009).Few studies have investigated these topics in adolescents, of these studies, the majority are cross-sectional. Relevant longitudinal studies in this area are less.

The 1946 British Birth Cohort (Mishra et al., 2003) explored longitudinal association between dietary vitamin E intake and blood pressure. The baseline data was collected in the year of 1950 when the participants were 4 years old. One follow-up was carried out in 1989 when the participants were 43 years old. The study found lower consumers of vitamin E in both childhood and adulthood were more likely to be hypertensive at mid-age (OR =1.8, 95%CI: 1.03 to 3.08), but a low intake of vitamin E at just one time point in either childhood or adulthood was not associated with a statistically significant increased risk of adulthood hypertension.

In children and adolescents, both observational studies and randomized controlled trial were found exploring the relationship between dietary fats intake and blood pressure (Aeberli et al., 2009, Mirza et al., 2013, Sugiyama et al., 2007, Ventura et al., 2008, Post et al., 1997, Setayeshgar et al., 2017a). In cross-sectional studies, higher total fat (Aeberli et al., 2009), MUFA (Aeberli et al., 2009, Sugiyama et al., 2007) and cholesterol (Smith and Franzen-Castle, 2012, Ventura et al., 2008) intake was linked with higher blood pressure, while SFA (Aeberli et al., 2009, Post et al., 1997) intake was found to be linked with lower blood pressure. One two-year longitudinal study was found in Canada (Setayeshgar et al., 2017a), where 448 students aged 10-17 years were observed. Dietary fat intake at baseline was linked with increased blood pressure levels between baseline and follow-up. In a two-year clinical train (Mirza et al., 2013), Hispanic children and adolescents received low-fat and low-glycemic-load diet had lower blood pressure levels than those who received normal diet. However, the results were rare and conflicted to the conclusion in adults (Schwingshackl et al., 2011, Appel et al., 2005, Yang et al., 2016), where SFA was found to be linked with increased blood pressure, and MUFA was found to be linked with decreased blood pressure.

It had been discussed in Chapter 1 that the progression of development of hypertension started at an early age of life in childhood, and will track into adulthood if there is no intervention given to control the blood pressure of children and adolescent. However, the studies on the longitudinal association between dietary factors and blood pressure in children and adolescents are lacking. Insufficient findings from previous studies support the need to carry out further exploration on this topic. In the ALSPAC study, blood pressure data, dietary data and potential confounders are available during the whole adolescent period. No previous analysis on diet and blood pressure in adolescents using ALSPAC data was found. Therefore, this study will add evidence to this area.

3.2 Aims

The aims of this chapter are to determine the longitudinal relationships between

a. early dietary vitamin E intake and later blood pressure levels and
b. early dietary fats intake and later blood pressure levels

in UK adolescents using ALSPAC dataset.

3.3 Methods

3.3.1 Sample and dataset

The whole ALSPAC dataset is held by the University of Bristol. Useful variables were selected from the complete variable list by 3 PhD researchers and then purchased from the University of Bristol. Participants completed questionnaires and/or attended clinical sessions at six age points as adolescents: namely 10, 11, 12, 13, 15 and 17 years old. Their parents were asked to complete relevant questionnaires at the same time. Participants with at least one valid blood pressure value were included in the current analysis. The exclusive criteria were those who were taking antihypertensive medication. Ethical approval for the ALSPAC was obtained for all the self-completed questionnaires and all clinic sessions from 2002 to 2008 .

3.3.2 Data collection

In ALSPAC, the following data were collected: general information, parents' history of hypertension, smoking and alcohol drinking habits, dietary data, measurements of weight, height and blood pressure. General information and parents' history of hypertension were collected at baseline from a postal self-completed questionnaire completed by the mothers of participants during pregnancy. Smoking and alcohol drinking habits were collected from postal self-completed questionnaires by the participants at age 10, 12, 13, 15 and 17 years. Dietary data were derived from a self-completed 4-day dietary diary at age 10 and 13, nutrients from supplements were included in the data. Weight and height were measured were measured by trained interviewers using a standard protocol at age 10, 11, 12, 13, 15 and 17 years.
Blood pressure was measured at age 10, 11, 12, 13, 15 and 17 years. Except for age 15 years, the readings were made using that standard protocol by a trained field workers. Participants was asked to sit quietly for at least 2 minutes before the measurement and during the measurement. At age 15 years, the still blood pressure was taken before an

ambulatory blood pressure measurement, using a different type of blood pressure monitor. Three measurements were taken in each session.

3.3.3 Data analysis

Energy and nutrient intakes were calculated based on the food consumption data from dietary records. BMI was calculated as weight (kg)/[height (m)]^2. BMI Z scores and height for age Z scores were calculated using British 1990 Growth Reference Charts (Cole et al., 1998).

In each session, blood pressure values from three measurements were recorded, and the mean of these three measurements were calculated for the final analysis. Both SBP and DBP were transformed to systolic or diastolic blood pressure Z-scores (SBPZ or DBPZ), based on age, gender and height data, according to *The Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents* (NHBPEP-working-group, 2004) , as recommended by the European Hypertension Society.

In this chapter, hypertension in adolescents is defined as SBP and/or DBP ≥95th percentile (equals to Z-score ≥1.645). This definition is based on *The Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents* (NHBPEP-working-group, 2004) and *The British Hypertension Society Guidelines* (Williams et al., 2004).

3.3.4 Statistical analysis

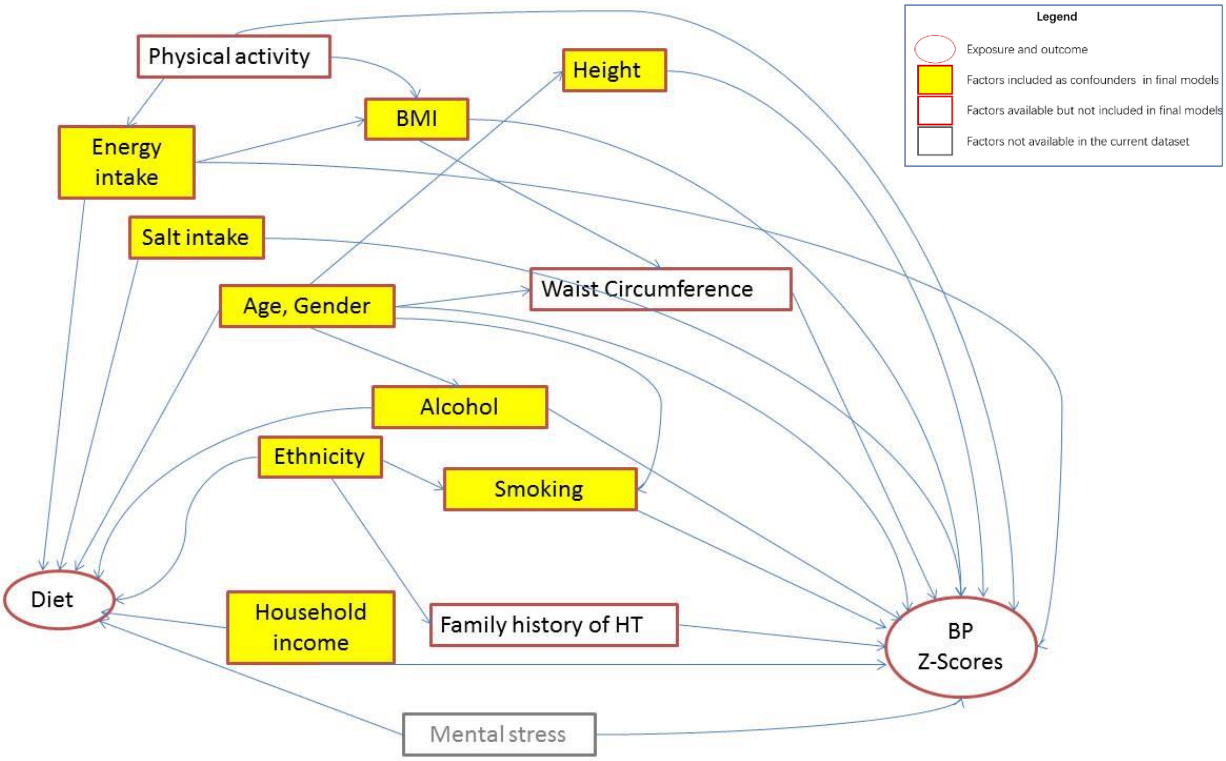
STATA/SE 13.1 for Windows was used to conduct all the statistical analysis. The level of statistical significance was $p<0.05$. All data were generally normally distributed, therefore data was described using mean, standard deviation and 95% confidence intervals.

Longitudinal associations between vitamin E levels, fat levels and future blood pressure levels

Linear regression for continuous outcomes (SBP, DBP, SBPZ and DBPZ) was undertaken to explore the associations. In addition, logistic regression for binary outcomes (hypertension v.s. normal blood pressure) was undertaken. For each exposure and outcome, one univariable model (Model 1) and one multivariable model (Model 2) adjusting for different confounders adjusted were created. Confounders were selected

according to a specifically designed Directed Acyclic Graph (DAG) (Figure 3.1) and previous studies.

Figure 3.1 Directed Acyclic Graph (DAG) of the ALSPAC analysis



The exposure factors were:

a. Dietary vitamin E intake (g) at age 10 and 13 years
b. Dietary fats intake at age 10 and 13 years: total fat (g), saturated fatty acids (g), monounsaturated fatty acids (g), polyunsaturated fatty acids (g), trans fatty acids (g), full-fat polyunsaturated margarine (g), low-fat polyunsaturated margarine (g), full-fat non-polyunsaturated margarine (g), low-fat non-polyunsaturated margarine (g), polyunsaturated cooking fat (g), non-polyunsaturated cooking fat (g).

The outcome factors were:

a. Blood pressure values: systolic blood pressure, diastolic blood pressure
b. Blood pressure Z-scores: systolic blood pressure Z-scores, diastolic blood pressure Z-scores
c. Risk of hypertension

The confounders in each model were:

Model 1 (M1): unadjusted.

Model 2 (M2): Gender, ethnicity, BMI, alcohol intake, smoking status, sodium intake, energy intake (excluding fat in models related to fat intake), parents' hypertension history and household income.

Survival analysis

Cox regression was used to find the association between dietary vitamin E/fats at age 10 or 13 years and risk of hypertension. The confounders in each model were:

Model 1 (M1): unadjusted.

Model 2 (M2): Gender, ethnicity, BMI, alcohol intake, smoking status, sodium intake, energy intake (excluding fat in models related to fat intake), parents' hypertension history and household income.

3.4 Results

3.4.1 General information

Total sample size of the ALSPAC population was 15,445, of which 6,655 of them were excluded due to missing blood pressure values. 8790 of them had at least one valid blood pressure value. None of the participants reported taking antihypertensive medication. General information was generally comparable between samples missing blood pressure value, samples with valid normal blood pressure values, and samples with at least one high blood pressure value. (Table 3.1)

General information for the participants that attended the survey at each age point is displayed in Table 3.2. Although ethnicity and household income data were only obtained at baseline, the composition of these factors were slightly changed as the participants attended at each session were not all the same. The percentage of participants that had ever drunk alcohol and smoked increased steadily during the studied years. The percentage of participants that ever drunk alcohol increased from 1.8% to 80.2% and the percentage of participants that ever smoked increased from 1.3% to 43.2%.

3.4.2 Anthropometric data, blood pressure levels and prevalence of hypertension in each age point

Height, weight and BMI increased with age, however, height for age Z-scores and BMIZ remained steady. Increasing trends could be seen with both systolic and diastolic blood pressure values, while no increasing trend was found in the prevalence of hypertension. Blood pressure at age 15 years was higher than at other age points. Approximately 10% of the participants were defined as hypertensive. At age 15 years the percentage was the highest (35.5%). (Table 3.3)

Table 3.1 General Information of all samples

Items	Total	Samples missing all blood pressure	Samples with at least one valid blood pressure
N(%)	15445(100%)	6655(43.1%)	8790(56.9%)
Gender [n(%)]			
Male	7635(49.4%)	3313(49.8%)	4322(49.2%)
Female	7219(46.7%)	2757(41.4%)	4462(50.8%)
Missing	591(3.8%)	585(8.8%)	6(0.1%)
Ethnicity [n(%)]			
White	11537(74.7%)	4144(62.3%)	7393(84.1%)
Other groups	613(4.0%)	276(4.1%)	337(3.8%)
Missing	3295(21.3%)	2235(33.6%)	1060(12.1%)
Total household income in last 12 months [n(%)]			
Under £20,000	2800(18.1%)	405(6.1%)	2395(27.2%)
£20,000-£34,999	1464(9.5%)	154(2.3%)	1310(14.9%)
£35,000-£44,999	1351(8.7%)	126(1.9%)	1225(13.9%)
£50,000 or more	934(6.0%)	110(1.7%)	824(9.4%)
Missing	8896(57.6%)	5860(88.1%)	3036(34.5%)
Ever drunk alcohol [n(%)]	6611(42.8%)	42(0.6%)	6569(74.7%)
Ever smoked [n(%)]	3551(23.0%)	24(0.4%)	3527(40.1%)

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Table 3.2 General Information at each age point

Items	Age 10	Age 11	Age 12	Age 13	Age 15	Age 17
N	7,188	7,036	6,647	5,366	5,305	4,663
Ethnicity [n (%)]						
White	6440(89.6%)	6304(89.6%)	5965(89.7%)	4843(90.3%)	4774(90%)	4125(88.5%)
Other groups	118(1.6%)	120(1.7%)	113(1.7%)	83(1.5%)	97(1.8%)	90(1.9%)
Missing	630(8.8%)	612(8.7%)	569(8.6%)	440(8.2%)	434(8.2%)	448(9.6%)
Total household income in last 12 months [n (%)]						
Under £20,000	1544(21.5%)	1533(21.8%)	1420(21.4%)	1142(21.3%)	1082(20.4%)	880(18.9%)
£20,000-£34,999	1751(24.4%)	1738(24.7%)	1647(24.8%)	1361(25.4%)	1330(25.1%)	1144(24.5%)
£35,000-£44,999	1107(15.4%)	1085(15.4%)	1065(16%)	876(16.3%)	876(16.5%)	749(16.1%)
£50,000 or more	731(10.2%)	744(10.6%)	702(10.6%)	605(11.3%)	608(11.5%)	536(11.5%)
Missing	2055(28.6%)	1936(27.5%)	1813(27.3%)	1382(25.8%)	1409(26.6%)	1354(29%)
Ever drunk alcohol [n (%)]	127(1.8%)	-	2035(30.6%)	2829(52.7%)	4444(83.8%)	3738(80.2%)
Ever smoked [n (%)]	94(1.3%)	-	833(12.5%)	1041(19.4%)	1652(31.3%)	2015(43.2%)

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Table 3.3 Anthropometrics data, blood pressure levels and prevalence of hypertension

	Age 10	Age 11	Age 12	Age 13	Age 15	Age 17
N	7,188	7,036	6,647	5,366	5,305	4,663
Mean Age (years)	10.1±0.3	11.1±0.3	12.2±0.4	13.2±0.4	15.1±0.3	17.2±0.5
Gender						
(Female/Male)	3529/3659	3454/3582	3261/3386	2644/2722	2510/2795	2062/2601
Mean Weight (kg)	38.1±8.6	43.8±10.2	49.3±10.9	54.5±11.2	61.6±11.9	67±13.8
BMI	18.2±3.1	19.1±3.5	19.8±3.5	20.3±3.5	21.5±3.6	22.8±4.2
BMIZ	0.3±1.2	0.4±1.2	0.3±1.2	0.3±1.1	0.4±1.1	0.4±1.2
Mean height (cm)	144±6.7	150.8±7.3	157.3±7.6	163.4±7.8	169.2±8.4	171.2±9.3
HAZ	0.3±1	0.4±1	0.4±1	0.4±1	0.3±1	0.3±1
SBP (mmHg)	104.2±9.1	105.5±9.9	111.3±9.7	106.5±9.4	122.9±10.9	114.4±9.8
SBPZ	0.1±0.9	0±0.9	0.3±0.9	-0.3±0.9	0.8±1	-0.5±0.9
DBP (mmHg)	60.1±8	58.8±6.6	56.7±7.9	57.6±6	67.4±8.8	64.4±6.3
DBPZ	-0.1±0.7	-0.3±0.6	-0.5±0.7	-0.5±0.5	0.2±0.8	-0.4±0.6
Hypertension [n(%)]	769(10.7%)	694(9.9%)	803(12.8%)	398(7.7%)	1389(35.3%)	354(9.2%)

BMI: body mass index BIMZ: body mass index z-score HAZ: height for age z-score

SBP: systolic blood pressure SBPZ: systolic blood pressure z-score DBP: diastolic blood pressure DBPZ: diastolic blood pressure z-score

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3.4.3 Energy and nutrients intake

Total energy intake increased from 7792 ±1591 kj/day at age 10 years to 8205 ±2168 kj/day at age 13 years, and sodium intake increased from 2570 ±689 mg/day at age 10 years to 2692 ± 881 mg/day at age 13 years. Vitamin E intake was 9.15 ± 3.74 mg/d at age 10 years and 9.23 ± 4.16 mg/d at age 13 years, the mean values were both higher than the reference intake for the UK (Institute of Medicine. Standing Committee on the Scientific Evaluation of Dietary Reference et al., 2003). The intakes of total fat, SFA, MUFA, PUFA, TFA and full-fat NPU margarine were increased, while the intakes of full-fat PU margarine, low-fat PU margarine, low-fat NPU margarine and PU decreased. The intake of NPU cooking fat did not change. No significant differences were found between daily energy and nutrients intakes of normotensive and hypertensive participants at either age 10 or age 13 years. (Table 3.4 and

Table 3.5)

Table 3.4 Daily energy and nutrient intakes at age 10

Nutrients	Total	Hypertensive			Non-hypertensive			p value
		Mean±SD	95% CI		Mean±SD	95% CI		
Energy (kcal)	7792±1591.55	7681.7±1625.57	7566.2	7797.1	7799.2±1623.2	7759.2	7839.2	0.059
Sodium (mg)	2570.6±689.66	2542.5±699.04	2492.8	2592.1	2582±705.45	2564.6	2599.3	0.144
Vitamin E (mg)	9.1±3.74	9.0±3.68	8.7	9.2	9.2±3.8	9.1	9.3	0.180
Total fat (g)	75.3±19.75	74.6±20	73.2	76.0	75.4±20.08	74.9	75.9	0.268
SFA (g)	29.2±9.28	28.7±9.04	28.1	29.3	29.1±9.48	28.9	29.4	0.242
MUFA (g)	25.7±7.1	25.5±7.4	25.0	26.0	25.8±7.25	25.6	26.0	0.286
PUFA (g)	12.3±4.55	12.2±4.52	11.9	12.6	12.4±4.66	12.3	12.5	0.289
TFA (g)	2.6±1.04	2.6±1.05	2.5	2.6	2.6±1.04	2.6	2.6	0.178
Full-fat PU margarine (g)	5.8±8.37	5.7±8.14	5.2	6.3	5.9±8.49	5.7	6.1	0.664
Low-fat PU margarine (g)	0.2±1.75	0.2±1.5	0.1	0.3	0.2±1.67	0.2	0.2	0.594
Full-fat NPU margarine (g)	2.9±6.29	3±6.62	2.5	3.5	2.8±6.29	2.6	3.0	0.388
Low-fat NPU margarine (g)	0.5±2.95	0.6±3.24	0.4	0.8	0.5±2.89	0.4	0.6	0.459
PU cooking fat (g)	0.5±1.43	0.6±1.37	0.5	0.6	0.5±1.37	0.5	0.6	0.566
NPU cooking fat (g)	0.1±0.48	0.1±0.41	0.0	0.1	0.1±0.43	0.0	0.1	1.000

SFA: saturated fatty acid MUFA: Monounsaturated fatty acids PUFA: polyunsaturated fatty acids, TFA: trans fatty acid

PU: polyunsaturated NPU:non- polyunsaturated

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Table 3.5 Daily energy and nutrient intakes at age 13

Nutrients	Total	Hypertensive			Non-hypertensive			p value
		Mean±SD	95% CI		Mean±SD	95% CI		
Energy (kcal)	8205.5±2168.01	8101±2244.46	7878.2	8323.9	8192.8±2156.03	8131.3	8254.3	0.420
Sodium (mg)	2692.1±881.03	2664.6±869.8	2578.3	2751	2687.3±880.17	2662.2	2712.4	0.623
Vitamin E (mg)	9.2±4.16	9.2±4.54	8.8	9.7	9.1±4.13	9	9.3	0.716
Total fat (g)	77.6±25.37	77.5±27.3	74.8	80.2	77.6±25.24	76.9	78.3	0.948
SFA (g)	29.3±11.65	28.9±12.48	27.7	30.2	29.3±11.6	29	29.7	0.509
MUFA (g)	26.1±9.19	26.3±9.77	25.3	27.3	26.1±9.16	25.8	26.4	0.683
PUFA (g)	13±5.62	13.2±6.03	12.6	13.8	13±5.53	12.8	13.1	0.387
TFA (g)	2.7±1.29	2.7±1.48	2.5	2.8	2.7±1.28	2.6	2.7	0.730
Full-fat PU margarine (g)	4.8±8.47	4.7±8.91	3.9	5.6	4.7±8.36	4.5	4.9	0.925
Low-fat PU margarine (g)	0.1±1.23	0.1±1.02	0.0	0.2	0.1±1.31	0.1	0.2	0.374
Full-fat NPU margarine (g)	3.1±7	3.3±7.33	2.6	4.1	3.1±6.89	2.9	3.3	0.501
Low-fat NPU margarine (g)	0.3±2.22	0.4±2.35	0.2	0.6	0.3±2.17	0.2	0.3	0.332
PU cooking oil (g)	0±0.37	0±0.38	0.0	0.1	0±0.35	0	0.0	0.722
NPU cooking oil (g)	0.1±0.5	0.1±0.75	0.0	0.1	0.1±0.47	0	0.1	0.638

SFA: saturated fatty acid MUFA: Monounsaturated fatty acids PUFA: polyunsaturated fatty acids, TFA: trans fatty acid

PU: polyunsaturated NPU:non- polyunsaturated

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3.4.4 Associations between dietary vitamin E intake and blood pressure levels

In the adjusted linear regression analysis, every 1mg increase in daily vitamin E intake at age 10 years was associated with 0.127 (95%CI: 0.015 to 0.240) mmHg higher DBP (p=0.026) at age 12 years, was associated with 0.251 (95%CI: 0.040 to 0.463) higher DBPZ (p=0.020) at age 15 years, and was associated with 0.207 (95%CI: 0.027 to 0.387) higher SBPZ (p=0.024) at age 17 years (Table 3.6). Every 1mg increase in daily vitamin E intake at age 13 years was associated with 0.270 (95%CI: 0.063 to 0.478) higher SBPZ (p=0.011) at age 17 years (Table 3.7).

Table 3.6 Relationship between daily dietary vitamin E intake at age 10 and later blood pressure values

Age	Change in BP per unit change in dietary Vita E intake							
	Non-adjusted models				Fully-adjusted models †			
	Coefficient	95%CI		P value	Coefficient	95%CI		P value
With systolic blood pressure (mmHg)								
Age 11	0.103	0.039	0.166	0.002*	0.048	-0.048	0.144	0.327
Age 12	0.095	0.031	0.160	0.004*	0.006	-0.121	0.132	0.930
Age 13	0.075	0.004	0.146	0.038*	-0.065	-0.169	0.039	0.222
Age 15	0.108	0.026	0.190	0.010*	-0.085	-0.269	0.098	0.361
Age 17	0.211	0.130	0.292	0.000*	-0.017	-0.124	0.090	0.753
With diastolic blood pressure (mmHg)								
Age 11	0.020	-0.022	0.063	0.342	0.049	-0.017	0.115	0.146
Age 12	0.079	0.026	0.131	0.003*	0.127	0.015	0.240	0.026*
Age 13	0.018	-0.026	0.063	0.422	0.040	-0.028	0.108	0.253
Age 15	0.116	0.049	0.182	0.001*	0.126	-0.032	0.283	0.118
Age 17	0.024	-0.027	0.076	0.355	0.028	-0.053	0.110	0.496
With systolic blood pressure Z-scores								
Age 11	0.004	-0.002	0.010	0.225	0.060	-0.116	0.237	0.503
Age 12	0.004	-0.002	0.010	0.197	-0.063	-0.249	0.123	0.506
Age 13	0.003	-0.004	0.010	0.363	0.017	-0.182	0.215	0.867
Age 15	0.004	-0.004	0.012	0.314	0.131	-0.030	0.291	0.112
Age 17	0.015	0.007	0.023	0.000	0.207	0.027	0.387	0.024*
With diastolic blood pressure Z-scores								
Age 11	-0.001	-0.005	0.003	0.549	0.159	-0.104	0.422	0.235
Age 12	0.005	0.000	0.010	0.036*	0.013	-0.205	0.232	0.905
Age 13	0.000	-0.004	0.004	0.888	-0.027	-0.328	0.275	0.863
Age 15	0.009	0.003	0.015	0.004*	0.251	0.040	0.463	0.020*
Age 17	-0.001	-0.006	0.004	0.623	0.055	-0.219	0.329	0.694

*p<0.005 in linear regression † Adjusted for : gender, ethnicity, BMI, alcohol intake, smoking status, sodium intake, energy intake, parents hypertension history and household income

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Table 3.7 Relationship between daily dietary vitamin E intake at age 13 and later blood pressure values

Age	Change in BP per unit change in dietary Vita E intake							
	Non-adjusted models				Fully-adjusted models †			
	Coefficient	95%CI		P value	Coefficient	95%CI		P value
With systolic blood pressure (mmHg)								
Age 15	0.094	0.019	0.168	0.013*	-0.081	-0.228	0.067	0.283
Age 17	0.190	0.115	0.264	0.000*	0.050	-0.036	0.136	0.252
With diastolic blood pressure (mmHg)								
Age 15	0.016	-0.044	0.076	0.592	-0.097	-0.223	0.028	0.128
Age 17	-0.013	-0.060	0.035	0.606	0.014	-0.052	0.079	0.680
With systolic blood pressure Z-scores								
Age 15	0.004	-0.003	0.011	0.292	0.173	-0.012	0.357	0.067
Age 17	0.014	0.007	0.022	0.000*	0.270	0.063	0.478	0.011*
With diastolic blood pressure Z-scores								
Age 15	-0.002	-0.007	0.004	0.564	-0.055	-0.299	0.189	0.657
Age 17	-0.003	-0.008	0.002	0.214	-0.004	-0.319	0.311	0.981

*p<0.005 in linear regression

† Adjusted for gender, ethnicity, BMI, alcohol intake, smoking status, sodium intake, energy intake, parents hypertension history and household income

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In logistic regression analysis, higher daily vitamin E intake at age 10 was found to be linked with higher risk of hypertension at age 17 years (OR=1.119, 95%CI: 1.004 to 1.247, p=0.043) (Table 3.8). Higher daily vitamin E intake at age 13 was found to be linked with lower risk of hypertension at age 15 years (OR=0.952, 95%CI: 0.913 to 0.992, p=0.020), but was linked with higher risk of hypertension at age 17 years (OR=1.112, 95%CI: 1.036 to 1.194, p=0.003) (Table 3.9).

Table 3.8 Daily dietary vitamin E intake at age 10 and later risk of hypertension

Age	Non-adjusted models				Fully-adjusted models †			
	OR	95%CI		P value	OR	95%CI		P value
With hypertension								
Age 11	0.989	0.967	1.011	0.330	1.004	0.954	1.056	0.889
Age 12	1.006	0.986	1.027	0.551	1.038	0.977	1.102	0.224
Age 13	1.000	0.972	1.030	0.976	1.028	0.955	1.107	0.467
Age 15	1.011	0.993	1.030	0.227	0.968	0.920	1.018	0.202
Age 17	1.018	0.985	1.051	0.286	1.119	1.004	1.247	0.043*
Ever had hypertension	1.019	0.989	1.048	0.214	1.001	0.957	1.048	0.955

*p<0.005 in logistic regression

† Adjusted for : gender, ethnicity, BMI, alcohol intake, smoking status, sodium intake, energy intake, parents hypertension history and household income

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Table 3.9 Daily dietary vitamin E intake at age 13 and later risk of hypertension

Age	Non-adjusted models				Fully-adjusted models †			
	OR	95%CI		P value	OR	95%CI		P value
With hypertension								
Age 15	1.014	0.997	1.031	0.102	0.952	0.913	0.992	0.020*
Age 17	1.048	1.019	1.078	0.001	1.112	1.036	1.194	0.003*
Ever had hypertension	1.032	1.006	1.058	0.014	0.993	0.957	1.030	0.689

*p<0.005 in logistic regression † Adjusted for : gender, ethnicity, BMI, alcohol intake, smoking status, sodium intake, energy intake, parents hypertension history and household income

In cox regression, the hazard ratio of medium-vitamin-E-intake group was significantly higher than the low-vitamin-E-intake group in both age 10 years (HR=1.340, 95% CI: 1.035 to 1.735, p=0.026) and age 13 years (HR=1.517, 95% CI: 1.122 to 2.052, p=0.007), see Table 3.10.

Table 3.10 Cox regression

Vitamin E level	Non-adjusted models				Fully-adjusted models †			
	HR	95%CI		P value	HR	95%CI		P value
Age 10								
Medium	1.047	0.901	1.217	0.550	1.340	1.035	1.735	0.026*
High	1.009	0.837	1.216	0.927	1.280	0.922	1.777	0.140
Age 13								
Medium	1.085	0.910	1.293	0.363	1.517	1.121	2.052	0.007*
High	1.026	0.828	1.271	0.818	1.402	0.959	2.048	0.081

*p<0.005 in cox regression

† Adjusted for gender, ethnicity, BMI, alcohol intake, smoking status, sodium intake, energy intake, parents hypertension history and household income

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3.4.5 Associations between dietary fats intake and blood pressure values

Total fat intake

In non-adjusted linear models, higher dietary total fat intake at age 10 years was linked with higher SBP at age 11, 12, 13, 15 and 17 years old, was linked with higher DBP at age 15 years old, and was linked with higher SBPZ at age 15 and 17 years old. However, in the adjusted models, every 1mg increase in daily total fat intake at age 10 years was only linked with 0.090 (95%CI: 0.025 to 0.155) mmHg higher SBP (p=0.007) at age 12 years old, and was associated with 0.008 (95%CI: 0.002 to 0.014) higher SBPZ (p=0.009) at age 12 years old (Table 3.11).

In non-adjusted models, higher dietary total fat intake at age 13 years is linked with higher SBP, DBP, SBPZ and DBPZ at age 15 and 17 years, except with higher DBPZ at age 15 years old. In adjusted models, every 1mg increase in daily total fat intake at age 13 years was only associated with 0.037 (95%CI: -0.037 to -0.066) mmHg lower SBP (p=0.011) at age 15 years (Table 3.12).

Table 3.11 Relationship between daily dietary total fat intake at age 10 and later blood pressure levels

Age	Change in BP per unit change in dietary fat intake							
	Non-adjusted models				Fully-adjusted models†			
	Coefficient	95%CI		P value	Coefficient	95%CI		P value
With systolic blood pressure (mmHg)								
Age 11	0.017	0.005	0.029	0.006*	0.060	-0.013	0.133	0.107
Age 12	0.024	0.012	0.036	0.000*	0.090	0.025	0.155	0.007*
Age 13	0.022	0.009	0.035	0.001*	0.027	-0.046	0.101	0.464
Age 15	0.045	0.029	0.060	<0.001*	0.022	-0.052	0.097	0.557
Age 17	0.072	0.056	0.087	<0.001*	0.038	-0.017	0.094	0.175
With diastolic blood pressure (mmHg)								
Age 11	0.003	-0.005	0.011	0.504	0.011	-0.036	0.059	0.643
Age 12	0.006	-0.004	0.016	0.254	0.015	-0.045	0.075	0.627
Age 13	-0.001	-0.009	0.007	0.813	0.013	-0.037	0.063	0.602
Age 15	0.017	0.004	0.029	0.009*	-0.014	-0.078	0.050	0.666
Age 17	-0.001	-0.011	0.009	0.873	0.012	-0.031	0.056	0.577
With systolic blood pressure Z-scores								
Age 11	0.000	-0.001	0.001	0.938	0.005	-0.002	0.012	0.145
Age 12	0.001	0.000	0.002	0.127	0.008	0.002	0.014	0.009*
Age 13	0.001	0.000	0.002	0.143	0.002	-0.005	0.009	0.532
Age 15	0.003	0.001	0.004	0.001*	0.001	-0.006	0.009	0.683
Age 17	0.006	0.004	0.007	<0.001*	0.003	-0.002	0.008	0.288

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With diastolic blood pressure Z-scores								
Age 11	-0.001	-0.001	0.000	0.115	0.001	-0.001	0.002	0.371
Age 12	0.000	-0.001	0.001	0.884	0.001	-0.004	0.005	0.767
Age 13	-0.001	-0.001	0.000	0.130	0.001	-0.004	0.006	0.710
Age 15	0.001	0.000	0.002	0.166	0.001	-0.003	0.005	0.667
Age 17	-0.001	-0.002	0.000	0.085	-0.002	-0.007	0.004	0.567

*p<0.05 in linear regression

† Age, sex, energy intake excluding fats, sodium intake, height, BMI category, smoking, alcohol intake, SES, ethnicity were adjusted in all final models.

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Table 3.12 Relationship between daily dietary total fat intake at age 13 and later blood pressure levels

Age	Change in BP per unit change in dietary fat intake							
	Non-adjusted models				Fully-adjusted models †			
	Coefficient	95%CI		P value	Coefficient	95%CI		P value
With systolic blood pressure (mmHg)								
Age 15	0.026	0.014	0.038	<0.001*	-0.037	-0.066	-0.007	0.014*
Age 17	0.058	0.046	0.070	<0.001*	-0.005	-0.024	0.014	0.602
With diastolic blood pressure (mmHg)								
Age 15	0.012	0.002	0.022	0.019*	0.004	-0.029	0.020	0.715
Age 17	-0.017	-0.025	-0.009	<0.001*	-0.004	-0.018	0.010	0.572
With systolic blood pressure Z-scores								
Age 15	0.001	0.000	0.003	0.023*	-0.003	-0.005	0.000	0.075
Age 17	0.005	0.004	0.006	<0.001*	-0.001	-0.002	0.001	0.571
With diastolic blood pressure Z-scores								
Age 15	0.000	-0.001	0.001	0.523	0.000	-0.002	0.002	0.795
Age 17	-0.002	-0.002	-0.001	<0.001*	0.000	-0.002	0.001	0.621

*p<0.05 in logistic regression

† Age, sex, energy intake excluding fats, sodium intake, height, BMI category, smoking, alcohol intake, SES, ethnicity were adjusted in all final models.

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In non-adjusted logistic regression analysis, higher dietary total fat intake at age 10 years was associated with higher risk of hypertension at age 15 years, but after adjusted for confounders, no significant association was found (Table 3.13). In non-adjusted models, higher dietary total fat intake at age 13 was associated with higher risk of hypertension at age 17 years, and also associated with higher risk of prevalence of hypertension from 13 to 17 years, but after adjusted for confounders, it was only associated with higher risk of hypertension at age 17 years (OR=1.015, 95%CI: 1.002 to 1.028, p=0.023) (Table 3.14).

Table 3.13 Daily dietary total fat intake at age 10 and later risk of hypertension

Age	Non-adjusted models				Fully-adjusted models †			
	OR	95%CI		P value	OR	95%CI		P value
With hypertension								
Age 11	0.996	0.992	1.000	0.063	1.001	0.992	1.011	0.825
Age 12	1.002	0.998	1.006	0.397	1.004	0.994	1.014	0.455
Age 13	1.002	0.997	1.008	0.385	1.003	0.989	1.018	0.661
Age 15	1.008	1.004	1.011	<0.001*	1.005	0.996	1.014	0.294
Age 17	1.004	0.998	1.010	0.189	0.995	0.978	1.012	0.565
Ever had hypertension	1.019	0.989	1.048	0.214	1.001	0.957	1.048	0.955

*p<0.005 in logistic regression

† Adjusted for: gender, ethnicity, BMI, alcohol intake, smoking status, sodium intake, energy intake excluding fat, parents hypertension history and household income

Table 3.14 Daily dietary total fat intake at age 13 and later risk of hypertension

Age	Non-adjusted models				Fully-adjusted models †			
	OR	95%CI		P value	OR	95%CI		P value
With hypertension								
Age 15	1.004	1.001	1.006	0.009	0.998	0.990	1.005	0.504
Age 17	1.009	1.004	1.013	0.001*	1.015	1.002	1.028	0.023*
Ever had hypertension	1.032	1.006	1.058	0.014*	0.993	0.957	1.030	0.689

*p<0.005 n logistic regression † Adjusted for : gender, ethnicity, BMI, alcohol intake, smoking status, sodium intake, energy intake excluding fat, parents hypertension history and household income

In survival analysis (cox regression), in the non-adjusted models, no significant association was found. After adjusted for confounders, the hazard ratio of the medium-fat-intake group was significantly higher than the low-fat-intake group in both age 10 years (HR=1.340, 95% CI: 1.035 to 1.735, p=0.026) and age 13 years (HR=1.517, 95% CI: 1.122 to 2.052, p=0.007) (Table 3.15)

Table 3.15 Cox regression (fat)

Fat intake level	Non-adjusted models				Fully-adjusted models †			
	HR	**95%CI**		**P value**	**HR**	**95%CI**		**P value**
Age 10								
Medium	1.047	0.901	1.217	0.550	1.340	1.035	1.735	0.026*
High	1.009	0.837	1.216	0.927	1.280	0.922	1.777	0.140
Age 13								
Medium	1.085	0.910	1.293	0.363	1.517	1.121	2.052	0.007*
High	1.026	0.828	1.271	0.818	1.402	0.959	2.048	0.081

*p<0.005 in cox regression

† Adjusted for: gender, ethnicity, BMI, alcohol intake, smoking status, sodium intake, energy intake excluding fat, parents hypertension history and household income

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Saturated fatty acids intake

In non-adjusted liner regression models, higher dietary saturated fatty acids intake at age 10 years was related with higher SBP at age 13 (coefficient=0.036, 95% CI: 0.007 to 0.064, p=0.014), 15 (coefficient=0.075, 95% CI: 0.042 to 0.109, p<0.001*) and 17 (coefficient=0.139, 95% CI: 0.107 to 0.172, p<0.001), but after adjusted for confounders, the relationship only existed between dietary SFA intake at age 10 years and SBP at 17 years (coefficient=0.127, 95% CI: 0.023to 0.231, p=0.016*). In non-adjusted models, higher dietary saturated fatty acids intake at age 10 years was related with higher SBP and DBP at both age15 and 17 years, and related with higher SBPZ and DBPZ at 17 years old. After adjusted for confounders, no significant relationship remained. No significant association was found between dietary SFA intake at 13 years and future blood pressure levels (Detailed table for age 10 can be seen in Table 3.16, detailed table for age 13 can be seen in Appendix 1).

Table 3.16 Relationship between daily dietary saturated fatty acids intake at age 10 and later blood pressure levels

Age	Change in BP per unit change in dietary SFA intake							
	Non-adjusted models				Fully-adjusted models †			
	Coefficient	95%CI		P value	Coefficient	95%CI		P value
With systolic blood pressure (mmHg)								
11y	0.017	-0.009	0.042	0.203	0.117	-0.022	0.256	0.100
12y	0.024	-0.002	0.050	0.071	0.097	-0.027	0.221	0.125
13y	0.036	0.007	0.064	0.014*	0.053	-0.083	0.190	0.441
15y	0.075	0.042	0.109	<0.001*	0.012	-0.128	0.151	0.869
17y	0.139	0.107	0.172	<0.001*	0.127	0.023	0.231	0.016*
With diastolic blood pressure (mmHg)								
11y	0.003	-0.014	0.020	0.740	0.035	-0.055	0.125	0.447
12y	-0.005	-0.027	0.016	0.612	-0.032	-0.146	0.082	0.576
13y	-0.009	-0.027	0.009	0.341	0.005	-0.088	0.097	0.921
15y	0.012	-0.015	0.039	0.383	-0.079	-0.198	0.040	0.195
17y	-0.008	-0.029	0.013	0.447	0.008	-0.074	0.090	0.852
With systolic blood pressure Z-scores								
11y	-0.001	-0.003	0.001	0.388	0.009	-0.004	0.022	0.170
12y	0.000	-0.002	0.002	0.972	0.008	-0.003	0.019	0.170
13y	0.001	-0.001	0.004	0.299	0.003	-0.009	0.016	0.613
15y	0.004	0.001	0.007	0.013*	0.000	-0.014	0.013	0.945
17y	0.011	0.008	0.014	<0.001*	0.010	0.000	0.020	0.052

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With diastolic blood pressure Z-scores								
11y	-0.001	-0.003	0.001	0.184	0.002	-0.006	0.010	0.595
12y	-0.001	-0.003	0.001	0.148	-0.004	-0.014	0.006	0.480
13y	-0.002	-0.003	0.000	0.071	0.000	-0.009	0.008	0.910
15y	0.000	-0.003	0.002	0.777	-0.008	-0.019	0.003	0.145
17y	-0.002	-0.004	0.000	0.066	0.000	-0.008	0.007	0.907

*p<0.05 in linear regression

† Age, sex, energy intake excluding fats, sodium intake, height, BMI category, smoking, alcohol intake, SES, ethnicity were adjusted in all final models.

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In non-adjusted logistic regression analysis, higher dietary saturated fatty acids was associated no significant association was found between daily total fat intake at age 10 years and future risk of hypertension (Table 3.17). No significant association was found between dietary SFA intake at 13 years and future risk of hypertension (Detailed table for age 13 can be seen in Appendix 1)

Table 3.17 Daily dietary saturated fatty acids intake at age 10 and later risk of hypertension

Age	Non-adjusted models				Fully-adjusted models †			
	OR	95%CI		P value	OR	95%CI		P value
With hypertension								
11y	0.990	0.981	0.999	0.030*	1.045	0.995	1.098	0.076
12y	0.999	0.991	1.008	0.819	1.023	0.975	1.073	0.362
13y	1.003	0.992	1.015	0.606	0.984	0.900	1.076	0.722
15y	1.014	1.007	1.022	<0.001*	1.012	0.976	1.049	0.530
17y	1.011	0.998	1.024	0.090	1.073	0.941	1.224	0.292
Ever had hypertension	1.014	1.005	1.023	0.003*	1.013	0.972	1.055	0.544

*p<0.005 in logistic regression

† Adjusted for: gender, ethnicity, BMI, alcohol intake, smoking status, sodium intake, energy intake excluding fat, parents hypertension history and household income

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Monounsaturated fatty acid intake

In the adjusted linear regression analysis, every 1mg increase in daily MUFA intake at age 10 years was associated with 0.264 (95%CI: 0.096 to 0.432) mmHg higher SBP (p=0.002) at age 12 years, and was associated with 0.023 (95%CI: 0.008 to 0.039) higher SBPZ (p=0.003) at age 12 years (Table 3.18). No significant association was found between dietary MUFA intake at 13 years and future blood pressure levels (Detailed table for age 10 can be seen in Table 3.18, detailed table for 13 can be seen in Appendix 1).

Table 3.18 Relationship between daily dietary MUFA intake at age 10 and later blood pressure levels

Age	Change in BP per unit change in dietary MUFA intake							
	Non-adjusted models				Fully-adjusted models †			
	Coefficient	95%CI		P value	Coefficient	95%CI		P value
With systolic blood pressure								
11y	0.048	0.015	0.082	0.005*	0.148	-0.042	0.338	0.126
12y	0.066	0.032	0.100	0.000*	0.264	0.096	0.432	0.002*
13y	0.059	0.022	0.096	0.002*	0.075	-0.113	0.263	0.434
15y	0.118	0.075	0.162	0.000*	0.093	-0.104	0.291	0.354
17y	0.193	0.150	0.236	0.000*	0.107	-0.036	0.250	0.142
With diastolic blood pressure								
11y	0.009	-0.013	0.031	0.426	0.058	-0.065	0.180	0.357
12y	0.019	-0.008	0.047	0.170	0.061	-0.095	0.217	0.443
13y	-0.003	-0.026	0.021	0.806	0.067	-0.061	0.194	0.305
15y	0.041	0.006	0.076	0.023*	0.021	-0.149	0.190	0.811
17y	0.004	-0.023	0.032	0.765	0.067	-0.045	0.179	0.242
With systolic blood pressure Z-scores								
11y	0.000	-0.003	0.003	0.830	0.013	-0.004	0.031	0.143
12y	0.003	0.000	0.006	0.072	0.023	0.008	0.039	0.003*
13y	0.003	-0.001	0.006	0.119	0.006	-0.011	0.024	0.482
15y	0.007	0.002	0.011	0.002*	0.007	-0.011	0.026	0.439
17y	0.015	0.011	0.019	0.000*	0.009	-0.005	0.023	0.212

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With diastolic blood pressure Z-scores								
11y	-0.001	-0.003	0.001	0.193	0.004	-0.007	0.015	0.432
12y	0.000	-0.002	0.003	0.796	0.005	-0.009	0.018	0.517
13y	-0.001	-0.004	0.001	0.192	0.006	-0.006	0.017	0.339
15y	0.002	-0.001	0.005	0.233	0.001	-0.014	0.016	0.899
17y	-0.002	-0.004	0.001	0.221	0.005	-0.006	0.015	0.361

*p<0.05 in linear regression

† Age, sex, energy intake excluding fats, sodium intake, height, BMI category, smoking, alcohol intake, SES, ethnicity were adjusted in all final models.

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In logistic regression analysis, higher daily MUFA intake at age 10 years was found to be linked with higher risk of hypertension at age 11 years (OR=1.133, 95%CI: 1.058 to 1.213, p<0.001) and age 12 years (OR=1.105, 95%CI: 1.036 to 1.179, p=0.002) (Table 3.19). No significant association was found between dietary MUFA intake at 13 years and future risk of hypertesion (Detailed table for 13 can be seen in Appendix 1).

Table 3.19 Daily dietary MUFA intake at age 10 and later risk of hypertension

Age	Non-adjusted models				Fully-adjusted models †			
	OR	95%CI		P value	OR	95%CI		P value
With hypertension								
11y	0.992	0.981	1.004	0.208	1.133	1.058	1.213	<0.001*
12y	1.005	0.994	1.016	0.367	1.105	1.036	1.179	0.002*
13y	1.007	0.992	1.022	0.357	1.072	0.954	1.205	0.243
15y	1.019	1.009	1.029	<0.001*	1.053	0.999	1.109	0.052
17y	1.008	0.991	1.026	0.367	1.133	0.957	1.341	0.147
Ever had hypertension	1.026	1.014	1.038	<0.001*	1.012	1.000	1.025	0.058

*p<0.005 in logistic regression

† Adjusted for: gender, ethnicity, BMI, alcohol intake, smoking status, sodium intake, energy intake excluding fat, parents hypertension history and household income

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Polyunsaturated fatty acid intake

In the adjusted linear regression analysis, no significant association was found between daily PUFA intake at age 10 years and future blood pressure levels (Table 3.20). No significant association was found between dietary PUFA intake at 13 years and future blood pressure levels (Detailed table for age 13 can be seen in Appendix 1).

Table 3.20 Relationship between daily dietary PUFA intake at age 10 and later blood pressure levels

Age	Change in BP per unit change in dietary PUFA intake							
	Non-adjusted models				Fully-adjusted models †			
	Coefficient	95%CI		P value	Coefficient	95%CI		P value
With systolic blood pressure								
11y	0.096	0.043	0.148	<0.001*	0.107	-0.125	0.339	0.365
12y	0.107	0.054	0.160	<0.001*	0.200	-0.004	0.404	0.055
13y	0.072	0.014	0.130	0.014*	-0.008	-0.245	0.229	0.946
15y	0.134	0.067	0.201	<0.001*	0.061	-0.182	0.303	0.624
17y	0.178	0.111	0.244	<0.001*	0.038	-0.142	0.218	0.679
With diastolic blood pressure								
11y	0.010	-0.025	0.044	0.589	0.019	-0.131	0.168	0.807
12y	0.073	0.030	0.116	0.001*	0.066	-0.122	0.254	0.491
13y	0.000	-0.037	0.037	0.999	0.029	-0.132	0.190	0.725
15y	0.075	0.021	0.129	0.007*	0.016	-0.192	0.223	0.882
17y	0.009	-0.033	0.051	0.675	0.061	-0.080	0.202	0.393
With systolic blood pressure Z-scores								
11y	0.003	-0.002	0.008	0.282	0.011	-0.011	0.032	0.340
12y	0.005	0.000	0.010	0.041	0.019	0.000	0.037	0.051
13y	0.003	-0.003	0.008	0.354	0.002	-0.020	0.024	0.883
15y	0.007	0.001	0.014	0.027	0.006	-0.017	0.029	0.605
17y	0.012	0.005	0.019	<0.001*	0.004	-0.013	0.021	0.644

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With diastolic blood pressure Z-scores								
11y	-0.002	-0.006	0.001	0.131	0.002	-0.012	0.015	0.823
12y	0.004	0.000	0.008	0.028*	0.006	-0.011	0.022	0.496
13y	-0.001	-0.005	0.002	0.386	0.004	-0.011	0.018	0.610
15y	0.005	0.000	0.010	0.054	0.001	-0.017	0.020	0.875
17y	-0.002	-0.006	0.002	0.250	0.006	-0.007	0.019	0.364

*$p<0.05$ in linear regression

† Age, sex, energy intake excluding fats, sodium intake, height, BMI category, smoking, alcohol intake, SES, ethnicity were adjusted in all final models.

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In logistic regression analysis, higher daily PUFA intake at age 10 years was found to be linked with higher risk of hypertension at age 11 years (OR=1.108, 95%CI: 1.024 to 1.200, p<0.011) and age 12 years (OR=1.096, 95%CI: 1.021 to 1.178, p=0.011) (Table 3.21). Higher daily PUFA intake at age 13 years was found to be linked with higher risk of hypertension at age 17 years (OR=1.015, 95%CI: 1.002 to 1.028, p=0.023) (Detailed table for age 13 can be seen in Appendix 1)

Table 3.21 Daily dietary PUFA intake at age 10 and later risk of hypertension

Age	Non-adjusted models				Fully-adjusted models †			
	OR	95%CI		P value	OR	95%CI		P value
With hypertension								
11y	0.994	0.976	1.013	0.528	1.108	1.024	1.200	0.011*
12y	1.011	0.994	1.028	0.219	1.096	1.021	1.178	0.011*
13y	0.998	0.975	1.022	0.886	1.102	0.971	1.252	0.133
15y	1.016	1.000	1.031	0.043*	1.028	0.966	1.094	0.386
17y	1.015	0.988	1.042	0.270	1.195	0.996	1.434	0.056
Ever had hypertension	1.029	1.010	1.047	0.002*	1.012	1.000	1.025	0.058

*p<0.005 in logistic regression

† Adjusted for: gender, ethnicity, BMI, alcohol intake, smoking status, sodium intake, energy intake excluding fat, parents hypertension history and household income

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Trans fatty acid (TFA) intake

In the adjusted linear regression analysis, every 1mg increase in daily TFA intake at age 10 years was associated with 1.219 (95%CI: 0.135 to 2.303) mmHg higher SBP (p=0.028) at age 12 years (Table 3.22). No significant association was found between dietary TFA intake at 13 years and future blood pressure levels (Detailed table for age 13 can be seen in Appendix 1).

Table 3.22 Relationship between daily dietary TFA intake at age 10 and later blood pressure levels

Age	Change in BP per unit change in dietary TFA intake							
	Non-adjusted models				Fully-adjusted models †			
	Coefficient	95%CI		P value	Coefficient	95%CI		P value
With systolic blood pressure								
11y	0.109	-0.123	0.340	0.356	0.644	-0.571	1.860	0.298
12y	0.333	0.098	0.569	0.006*	1.219	0.135	2.303	0.028*
13y	0.402	0.147	0.657	0.002*	0.614	-0.588	1.817	0.316
15y	0.621	0.323	0.919	<0.001*	0.073	-1.169	1.316	0.908
17y	0.826	0.529	1.123	<0.001*	-0.273	-1.186	0.640	0.557
With diastolic blood pressure								
11y	-0.031	-0.185	0.123	0.695	0.186	-0.600	0.972	0.643
12y	0.028	-0.164	0.220	0.774	0.426	-0.575	1.426	0.404
13y	0.059	-0.102	0.220	0.471	0.464	-0.351	1.280	0.264
15y	0.311	0.071	0.552	0.011*	0.599	-0.461	1.660	0.267
17y	-0.105	-0.294	0.084	0.276	-0.013	-0.729	0.704	0.972
With systolic blood pressure Z-scores								
11y	-0.014	-0.036	0.008	0.217	0.031	-0.083	0.144	0.593
12y	0.008	-0.014	0.030	0.477	0.092	-0.007	0.191	0.069
13y	0.019	-0.005	0.043	0.119	0.026	-0.086	0.138	0.642
15y	0.034	0.005	0.062	0.022*	-0.027	-0.145	0.092	0.657
17y	0.057	0.028	0.087	<0.001*	-0.054	-0.141	0.034	0.227

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With diastolic blood pressure Z-scores								
11y	-0.015	-0.029	-0.001	0.039*	0.001	-0.070	0.071	0.979
12y	-0.010	-0.027	0.008	0.281	0.024	-0.064	0.113	0.590
13y	-0.005	-0.020	0.010	0.519	0.025	-0.047	0.098	0.493
15y	0.014	-0.008	0.036	0.201	0.036	-0.058	0.131	0.450
17y	-0.022	-0.040	-0.004	0.015*	-0.015	-0.081	0.052	0.665

*p<0.05 in linear regression

† Age, sex, energy intake excluding fats, sodium intake, height, BMI category, smoking, alcohol intake, SES, ethnicity were adjusted in all final models

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In logistic regression analysis, higher daily TFA intake at age 10 years was found to be linked with higher risk of hypertension at age 12 years (OR=1.526, 95% CI: 1.019 to 2.284, p<0.001) (Table 3.23). No significant association was found between dietary TFA intake at 13 years and future risk of hypertension (Detailed table for age 13 can be seen in Appendix 1).

Table 3.23 Daily dietary TFA intake at age 10 and later risk of hypertension

Age	Non-adjusted models				Fully-adjusted models †			
	OR	95%CI		P value	OR	95%CI		P value
With hypertension								
11y	0.959	0.884	1.040	0.312	1.052	0.665	1.666	0.827
12y	1.024	0.949	1.105	0.537	1.526	1.019	2.284	0.040*
13y	1.104	0.998	1.221	0.054	0.795	0.365	1.730	0.563
15y	1.114	1.042	1.191	0.001*	1.133	0.824	1.557	0.443
17y	1.121	0.997	1.262	0.057	1.180	0.440	3.169	0.742
Ever had hypertension	1.051	0.974	1.134	0.201	1.012	1.000	1.025	0.058

*p<0.005 in logistic regression

† Adjusted for: gender, ethnicity, BMI, alcohol intake, smoking status, sodium intake, energy intake excluding fat, parents hypertension history and household income

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PUFA cooking oil and margarine intake

In the adjusted linear regression analysis, no significant association was found between daily PUFA cooking oil and margarine intake at age 10 years and future blood pressure levels (Table 3.24). Every 1mg increase in daily PUFA cooking oil and margarine intake at age 13 years was associated with 0.157 (95%CI: 0.071 to 0.243) mmHg higher SBP ($p<0.001$), 0.107 (95%CI: 0.042 to 0.173) mmHg higher SBP ($p=0.001$), 0.017 (95%CI: 0.09 to 0.025) higher SBPZ ($p<0.001$) and 0.010 (95%CI: 0.004 to 0.016) higher DBPZ ($p=0.002$) at age 17 years (Detailed table for age 13 can be seen in Appendix 1).

Table 3.24 Relationship between daily dietary PUFA cooking oil and margarine intake at age 10 and later blood pressure levels

Age	Change in BP per unit change in PUFA cooking oil and margarine intake							
	Non-adjusted models				Fully-adjusted models †			
	Coefficient	95%CI		P value	Coefficient	95%CI		P value
With systolic blood pressure								
11y	0.035	0.007	0.062	0.013*	-0.022	-0.140	0.097	0.720
12y	0.025	-0.003	0.052	0.086	0.011	-0.096	0.117	0.845
13y	0.005	-0.026	0.035	0.758	0.027	-0.095	0.149	0.666
15y	0.018	-0.018	0.053	0.338	-0.084	-0.207	0.038	0.177
17y	0.031	-0.004	0.066	0.081	-0.007	-0.100	0.086	0.884
With diastolic blood pressure								
11y	0.009	-0.010	0.027	0.363	0.006	-0.070	0.083	0.870
12y	0.031	0.008	0.053	0.008*	0.017	-0.081	0.114	0.735
13y	-0.003	-0.022	0.016	0.765	0.039	-0.043	0.120	0.355
15y	0.040	0.011	0.069	0.007*	0.045	-0.059	0.150	0.394
17y	0.008	-0.014	0.030	0.489	0.027	-0.045	0.098	0.465
With systolic blood pressure Z-scores								
11y	0.002	0.000	0.005	0.114	0.000	-0.011	0.011	0.986
12y	0.002	-0.001	0.004	0.191	0.002	-0.007	0.012	0.629
13y	0.000	-0.003	0.003	0.874	0.004	-0.007	0.016	0.460
15y	0.001	-0.003	0.004	0.663	-0.006	-0.018	0.005	0.279
17y	0.003	-0.001	0.006	0.134	0.003	-0.007	0.012	0.579

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With diastolic blood pressure Z-scores								
11y	0.000	-0.001	0.002	0.749	0.002	-0.005	0.008	0.643
12y	0.002	0.000	0.004	0.021*	0.002	-0.006	0.011	0.614
13y	0.000	-0.002	0.002	0.860	0.004	-0.003	0.012	0.227
15y	0.004	0.001	0.006	0.006*	0.005	-0.005	0.014	0.313
17y	0.000	-0.002	0.002	0.938	0.004	-0.003	0.011	0.275

*$p<0.05$ in linear regression

† Age, sex, energy intake excluding fats, sodium intake, height, BMI category, smoking, alcohol intake, SES, ethnicity were adjusted in all final models

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In logistic regression analysis, higher daily PUFA cooking oil and margarine intake at age 10 years was found to be linked with higher risk of hypertension at age 17 years (OR=1.090, 95%CI: 1.034 to 1.149, p=0.001) (Table 3.25). Higher daily PUFA cooking oil and margarine intake at age 13 years was found to be linked with higher risk of hypertension at age 17 years (OR=1.132, 95%CI: 1.066 to 1.202, p<0.001) (Detailed table for age 13 can be seen in Appendix 1).

Table 3.25 Daily dietary PUFA cooking oil and margarine intake at age 10 and later risk of hypertension

Age	Non-adjusted models				Fully-adjusted models †			
	OR	95%CI		P value	OR	95%CI		P value
With hypertension								
11y	0.999	0.990	1.009	0.905	1.018	0.975	1.063	0.426
12y	1.006	0.997	1.015	0.186	1.035	0.998	1.074	0.064
13y	0.996	0.984	1.009	0.578	1.036	0.968	1.109	0.306
15y	1.000	0.992	1.008	0.918	0.977	0.947	1.008	0.143
17y	1.010	0.997	1.024	0.134	1.090	1.034	1.149	0.001*
Ever had hypertension	1.006	0.996	1.015	0.230	1.000	0.969	1.032	0.998

*p<0.005 in logistic regression

† Adjusted for: gender, ethnicity, BMI, alcohol intake, smoking status, sodium intake, energy intake excluding fat, parents hypertension history and household income

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Un-PUFA cooking oil and margarine intake

In the adjusted linear regression analysis, no significant association was found between daily un-PUFA cooking oil and margarine intake at age 10 years and future blood pressure levels (Table 3.26). No significant association was found between dietary un-PUFA cooking oil and margarine intake at 13 years and future blood pressure levels (Detailed table for age 13 can be seen in Appendix 1).

Table 3.26 Relationship between daily dietary Un-PUFA cooking oil and margarine intake at age 10 and later blood pressure levels

Age	Change in BP per unit change in dietary Un-PUFA cooking oil and margarine intake							
	Non-adjusted models				Fully-adjusted models †			
	Coefficient	95%CI		P value	Coefficient	95%CI		P value
With systolic blood pressure								
11y	0.025	-0.010	0.060	0.160	-0.072	-0.231	0.086	0.369
12y	0.018	-0.017	0.054	0.309	-0.025	-0.166	0.116	0.725
13y	0.037	-0.002	0.076	0.062	-0.038	-0.201	0.125	0.648
15y	0.052	0.007	0.097	0.022*	-0.020	-0.194	0.153	0.818
17y	0.026	-0.018	0.070	0.248	-0.106	-0.227	0.015	0.086
With diastolic blood pressure								
11y	0.020	-0.003	0.044	0.086	0.061	-0.042	0.163	0.246
12y	0.001	-0.028	0.030	0.927	-0.003	-0.132	0.126	0.964
13y	0.004	-0.021	0.028	0.763	0.003	-0.106	0.112	0.956
15y	0.012	-0.024	0.048	0.504	0.023	-0.125	0.170	0.763
17y	0.004	-0.024	0.032	0.779	-0.025	-0.118	0.068	0.592
With systolic blood pressure Z-scores								
11y	0.001	-0.002	0.005	0.446	-0.006	-0.021	0.008	0.389
12y	0.000	-0.003	0.004	0.886	-0.004	-0.017	0.009	0.578
13y	0.001	-0.002	0.005	0.451	-0.006	-0.021	0.009	0.440
15y	0.003	-0.002	0.007	0.210	-0.002	-0.019	0.014	0.789
17y	0.001	-0.004	0.005	0.800	-0.012	-0.023	0.000	0.052

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With diastolic blood pressure Z-scores								
11y	0.001	-0.001	0.003	0.304	0.005	-0.004	0.015	0.245
12y	-0.001	-0.003	0.002	0.698	-0.001	-0.012	0.011	0.893
13y	-0.001	-0.003	0.001	0.308	-0.001	-0.010	0.009	0.875
15y	0.001	-0.003	0.004	0.708	0.002	-0.012	0.015	0.803
17y	-0.001	-0.003	0.002	0.674	-0.003	-0.012	0.006	0.500

*p<0.05 in linear regression

† Age, sex, energy intake excluding fats, sodium intake, height, BMI category, smoking, alcohol intake, SES, ethnicity were adjusted in all final models

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In logistic regression analysis, no significant association was found between daily un-PUFA cooking oil and margarine intake at age 10 years and future risk of hypertension (Table 3.27). No significant association was found between dietary un-PUFA cooking oil and margarine intake at 13 years and future risk of hypertension (OR=1.015, 95%CI: 1.002 to 1.028, p=0.023) (Detailed table for age 13 can be seen in Appendix 1).

Table 3.27 Daily dietary Un-PUFA cooking oil and margarine intake at age 10 and later risk of hypertension

Age	Non-adjusted models				Fully-adjusted models †			
	OR	95%CI		P value	OR	95%CI		P value
With hypertension								
11y	1.019	1.008	1.030	0.001*	0.996	0.942	1.053	0.875
12y	1.009	0.998	1.020	0.109	0.965	0.906	1.028	0.274
13y	1.018	1.004	1.033	0.013*	0.994	0.906	1.090	0.894
15y	1.012	1.002	1.022	0.014*	1.019	0.976	1.063	0.398
17y	1.007	0.990	1.025	0.425	0.860	0.728	1.017	0.079
Ever had hypertension	1.011	1.000	1.023	0.054	1.007	0.958	1.058	0.784

*p<0.005 logistic regression

† Adjusted for: gender, ethnicity, BMI, alcohol intake, smoking status, sodium intake, energy intake excluding fat, parents hypertension history and household income

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3.5 Discussion

This study aimed to determine the associations between vitamin E, fats intake and blood pressure in UK adolescents using longitudinal data. Around 10% of the total sample were defined as hypertensive in the ALSPAC population. The rate was similar to that of UK national data (NDNS) as displayed in Chapter 2 and similar to that in other countries (Shatoor et al., 2011, Zhao et al., 2017, Larkins et al., 2017, Karatzi et al., 2017). Generally, both higher dietary intake of vitamin E and fats were associated with higher blood pressure levels 5 or 7 years later.

3.5.1 Vitamin E and future blood pressure

In ALSPAC population, higher vitamin E intakes at age 10 years were longitudinally associated with increased blood pressure values, and higher risk of hypertension. The results were opposite to that of the cross-sectional in Chapter 2, where higher dietary vitamin E intake was linked with lower blood pressure levels in adolescents. The results were also opposite to previous longitudinal study where higher vitamin E intake at both childhood and adulthood was linked with lower blood pressure levels as adult (Mishra et al., 2003). The study selected sample from the 1946 British Birth Cohort (Mishra et al., 2003). The participants were recruited in the year of 1950 when they were 4 years old, and then followed up 40 years later in the year of 1989. Twenty-four-hour and 48-hour dietary recalls were used respectively at these two time points to assess dietary data. The association was analysed using multiple regression, adjusted for gender, social class category, area of residence, exercise, smoking, PUFA index, BMI at age 43y, and dietary intake of vitamin C, b-carotene, calcium, sodium, potassium and magnesium in both childhood and adulthood. The duration between baseline and the follow-up was quite long, although no surveillance of the participants' diet was carried out during the studied time, high intake of vitamin E at both 4 years and at 43 years could imply that the participant had a long term dietary pattern rich in vitamin E. However, not including vitamin supplements in the dietary recall, variations in the accuracy of dietary assessment and food composition over the studied time could also introduce bias to the current result (Beaton et al., 1983). In summary, these results from the cross-sectional and longitudinal analysis suggested that dietary vitamin E could have a cross-sectional protective effect on blood pressure, which can be seen in adolescents, but the longitudinal effect might need longer exposure term (40 years) to appear when the participants turned to adults.

The invert result of vitamin E's effect on blood pressure might be caused by higher fat intake. Fat is high in vitamin E (2015a), and in ALSPAC adolescent data, higher intake of vitamin E was associated with higher intake of fat (in age 10 years: coef.=2.8, 95% CI 2.7 to 2.9, p<0.001; in age 13 years coef.=3.4, 95% CI 3.3 to 3.5, p<0.001).

The potential mechanism of how serum vitamin E decreases blood pressure are: as an peroxyl radical scavenger, vitamin E can prevent the propagation of free radicals in membranes and in plasma lipoproteins (Traber and Atkinson, 2007) and protect PUFA (Buettner, 1993). Vitamin E can also increase nitric oxide concentrations (Green et al., 1998) because of its anti-oxidant effect. Nitrogen monoxide was found to have acute effects on reducing blood pressure by increase vascular compliance (Houston and Hays, 2014), which may lead to the cross-sectional negative association between dietary vitamin E intake and lower blood pressure.

However, the effect of taking higher vitamin E from diet or supplements on cardiovascular health was not clear. The benefit of high dose of vitamin E intake (400 to 800 IU/d, equals to 267 to 534 mg/d) on cardiovascular disease was found in many trials in adults, especially in treating cardiovascular disease patients (Kushi et al., 1996, Stephens et al., 1996, Boaz et al., 2000, Boshtam et al., 2002, Rodrigo et al., 2008, Rimoldi et al., 2015), but some studies did not find significant associations (Rasool et al., 2003, Negri et al., 1994, Jialal and Devaraj, 2000). And recently some studies even found the harmful effect of taking high dose of vitamin E on cardiovascular health (Ward et al., 2007, Bjelakovic et al., 2013).

Therefore, further studies where more frequent follow-up data was collected in a longer observation time are needed to clarify the association between dietary vitamin E intake and blood pressure changes.

3.5.2 Dietary fats and future blood pressure

Overall, in the ALSPAC population, dietary fats intake is linked with higher future blood pressure levels to varying degrees. Higher total fat intake at age 10 years was associated with higher DBP at age 12 years, higher DBPZ at 15 years, higher SBPZ and higher risk of hypertension at 17 years; higher total fat intake at age 13 years was associated with higher SBPZ and higher risk of hypertension at 17 years. Higher SFA intake at age10 years was associated with higher SBP at age 17 years. Higher MUFA and PUFA intakes at age 10 years were both associated with higher risk of hypertension at age 11 years and 12 years, and were both associated with overall risk of prevalence

hypertension from 10 years to 17 years; higher MUFA intake at age 10 years was also associated with higher SBP and SBPZ at age 12 years; higher PUFA intake at age 13 was associated higher risk of hypertension at age 17 years. Higher TFA intake at age 10 years was associated with higher SBP and higher risk of hypertension at age 12 years. Higher PUFA cooking oil and margarine intake at age 10 years was associated with higher risk of hypertension at age 15; higher PUFA cooking oil and margarine intake at age 13 years was associated with higher risk of hypertension at age 15 years and 17 years, and was also associated with higher SBP, DBP, SBPZ and DBPZ at age 17 years. Only one negative association was found, higher total fat intake at age 13 years was associated with lower risk of hypertension at age 15 years.

These results agreed with previous cross-sectional studies in children and adolescents, where total fat (Aeberli et al., 2009) and MUFA (Aeberli et al., 2009, Sugiyama et al., 2007) were found to be linked with higher blood pressure levels, and also agreed with findings from a longitudinal study, where higher total fat intake was linked with higher blood pressure levels two years later (Setayeshgar et al., 2017a). However, the positive relationship of PUFA and blood pressure were conflicted to the conclusion in adult studies, where PUFA were found to have benefit effect on blood pressure and cardiovascular health (Appel et al., 1993, Geleijnse et al., 2002). Although higher fats intake, therefore higher energy intake, was partly associated with higher blood pressure levels (Mathew and Chary, 2013), higher PUFA intake still shows the protective effect of hypertension in some population. The potential mechanisms include: PUFA can 1) regulate vasomotor tone by decreasing the production of vasoconstrictor (Matsumoto et al., 2009), 2) increase renal sodium excretion by increases the glomerular filtration rate, which could be mediated by an increased availability of renal prostaglandins (Bernardi et al., 1986) and 3) work as anti-inflammatory factor (Attaman et al., 2014, Calder, 2015). PUFAs also reduce angiotensin-converting enzyme (ACE) activity, Tumor Growth Factor- beta (TGF-β) expression, angiotensin II formation, enhance endothelial nitric oxide (NO) generation (Zebrowska et al., 2015) and activate the parasympathetic nervous system. Therefore, vasodilation are improved and the arterial compliance of both small and large arteries are increased (Cicero et al., 2009). As arterial compliance is decreasing with aging (Benetos et al., 1993, Reneman et al., 1985), the above effect may not be significant in children and adolescents. This can explain the conflicting results between ALSPAC adolescents' analysis and previous studies in adults.

3.5.3 Selecting of confounders

The confounders that were included in each final model were determined using a DAG (Figure 3.1) and also referring to the confounders adjusted for in previous relevant studies. Age, gender, BMI, height and ethnicity were included as confounders in the majority of previous studies, therefore they were included in this analysis. Physical activity is linked with both blood pressure levels and diet, but it was not adjusted for in the final models, as it is in the same pathway with BMI and energy intake. Adjusting for all these three factors may cause over adjusting. Considering physical activity data was only available at one age point (13 years), while energy intake data is available at two age points (10 and 13 years) and BMI data is available at every age point, the physical activity was not included in the final models. Metal stress is a potential confounder in the relationship between diet and blood pressure levels, but it was not included in the final models as we don't have the metal stress data in our dataset. Not including this factor may cause biased results.

3.5.4 Strengths and Limitations

ALSPAC is a large longitudinal survey in the UK. High quality repeated measured data was collected in a long duration from both parents and children.

Compared to the national population, the sample generated in ALSPAC is under-representative of non-white population, this may affect the generalization of the result (Boyd et al., 2013). The main limitation of the study is that as a longitudinal study involving adolescents, keeping participants from dropping off is quite difficult. The response rate was keeping decreases at every clinic visit. However, it is still a sample large enough to run the analysis.

Although blood pressure data was collected at every age point, dietary data was derived only at age 10 and 13 years. As suggested by previous studies (Mishra et al., 2003, Boshtam et al., 2002, Aeberli et al., 2009, Mirza et al., 2013, Simons-Morton and Obarzanek, 1997, Setayeshgar et al., 2017a, Shi et al., 2014) and the cross-sectional findings in Chapter 2, dietary intake of vitamin E, fats, and other nutrients such as sodium may influence short term blood pressure. Therefore, future blood pressure value at 15 or 17 years might be influenced by the diet at that age. However, it is impossible to reduce these bias without dietary data collected at age 12, 15 and 17 years. The same issue applied to the confounders, for example, the social economic status data and

parents' history of hypertension were only collected at baseline. During the decades of follow-up, no updating of this information was recorded in ALSPAC. It is not possible to confirm these factors of the participants' remained the same during the studied time. The potential changes of diet and confounders could introduce bias to the existing results.

Contrary to other results, higher vitamin E and total fat intakes at age 13 years was both found to be linked with lower SBP or risk of hypertension at age 15 years. The method used to measure blood pressure at age 15 years was different from that at other age points. At age 15 years, the participants' blood pressure was measured in an ambulatory blood pressure measurement. Although the value was collected before doing exercise, the variation in equipment may cause variation in blood pressure readings. This will reduce the comparability of data at age 15 years and at other age points.

3.6 Conclusion

In the ALSPAC population, prevalence of hypertension was approximately 10% as they were adolescents. Higher dietary vitamin E intake was found to have longitudinal associations with increased later DBP, DBPZ, SBPZ and risk of hypertension. Higher dietary total fat intake at was found to have longitudinal associations with increased later SBP, SBPZ and risk of hypertension. Except when blood pressure level at age 15 is considered as an outcome, higher vitamin E and total fat intakes were found to be linked with lower SBP and/or lower risk of hypertension at that age.

Review of previous knowledge before starting Chapter 4 and 5

In the Introduction (Chapter 1), we discussed the necessity and utility of carrying out an online survey to explore the associations between diet and blood pressure in adolescents.

- The prevalence of hypertension in adolescents is increasing, and elevated blood pressure in adolescents predicts a higher chance of hypertension in adulthood.
- Diet is one of the important factors that can affect blood pressure levels in adolescents.
- The proportion of adolescents who use the Internet has been growing exponentially. Social networking websites are particularly popular among adolescents.
- Online research targeting children and adolescents has become more popular. Online recruitment through Facebook has been proven to be effective and cost-efficient by previous studies.
- Few studies were found to explore diet and blood pressure in adolescents using online technologies.

Chapter 4 and 5 describe the Online Research of Adolescents and Good Eating (the ORANGE study). In chapter 4, a valid method for adolescents to measure their own blood pressure was developed. This method was used in the online pilot survey.

Chapter 4. Developing and validating a blood pressure measuring method for an online survey in adolescents.

Abstract

Background: A standard method for the participants to measure their own blood pressure values was required in the online survey; however relevant studies are lacking in adolescents. The aims of this chapter are to develop and validate a blood pressure measuring method for an online survey in adolescents.

Methods: variance of methods of measuring blood pressure were reviewed. Smart phone applications which were designed to measure blood pressure were tested in a small pilot study. A method that composed of self-designed instruction and a low-price automatic blood pressure monitor was tested in 13 to 19 years old participants, who were recruited from local school students, visiting students on university open-days and first year students in the University of Leeds. The results from self-measurement were compared with the standard measurement using a paired t-test and Bland- Altman plot. A method was then selected after the review and testing.

Results and conclusion: None of the smart phone applications were found to provide accurate blood pressure readings. However, following our self-designed instruction and using the validated blood pressure monitor (Omron PL100), adolescents could measure their own blood pressure and provide blood pressure readings that had acceptable agreement with standard blood pressure values. The combination of Omron PL100 blood pressure monitor and our self-designed instructions were selected to be used in the future online survey.

4.1 Introduction

In the pilot online survey, we did not plan to do face-to-face interviews and we therefore needed to obtain the participants' accurate blood pressure values remotely. In order to achieve this, a standard method for the participants to measure their own blood pressure values was required. The development of the method includes information on how blood pressure monitors were selected and development of a standard measuring method. In this chapter, we a) reviewed available devices to measure blood pressure, b) chose the most appropriate one of them to use in the pilot online survey, c) designed an instruction leaflet for the adolescents to guide them to measure their own blood pressure, and d) tested the accuracy of self-measured blood pressure using the combination of the chosen blood pressure measuring device and the instruction leaflet.

4.1.1 Factors that affect blood pressure measurement in adolescents

When measuring blood pressure, the accuracy of the readings may be affected by several factors, including the equipment used in the measurement (Niyonsenga et al., 2008, Turner et al., 2006, Tolonen et al., 2015), the cuff size (Whincup et al., 1989, Mattoo, 2002, Irving et al., 2016, Arafat and Mattoo, 1999), observer errors (Neufeld and Johnson, 1986, de Lusignan et al., 2004, Rose, 1965), the time of the measurement (Bodegard et al., 2002, Bilo et al., 2018, Okutucu et al., 2011), the part of patient's body where the monitor is attached (Zweiker et al., 2000, Cuckson et al., 2004, Dieterle et al., 1998, Watson et al., 2017), the position of the body or arm of the patient (Eser et al., 2007, Netea et al., 2003, Byrd and Brook, 2014), and mental stress such as the "white coat" effect (Krmar, 2018, Sorof and Portman, 2000). These factors should be taken into consideration when assessing blood pressure levels.

Places to attach cuff when measuring blood pressure

Normally, there are two types of automated blood pressure monitors according to the place where the cuff is attached- upper arm or wrist. The upper arm type is more popular, and has been widely validated, while the wrist type seems more convenient to the patients as it is not necessary to take off outer clothing and expose the upper arm while measuring blood pressure. Also it does not require the selection of correct size of cuff (Cuckson et al., 2004). However, the wrist monitors are not recommended by the British Hypertension Society at the moment, based on the conflicting results from studies on the reliability of wrist type monitors (Cuckson et al., 2004, Plavnik and Zanella, 2001, Zweiker et al., 2000, Dieterle et al., 1998, Rogers et al., 1999). The

reason for this is that a wrist device may fulfil the accuracy criteria of a validation protocol when strict attention is paid to having the wrist at heart level but with home use this may not happen and as a consequence the measurement could be invalid .

White coat effect

The white coat effect, or white coat hypertension, is defined as an isolated elevation of blood pressure during clinical visits on at least three separate occasions, but normal blood pressure readings in other conditions. In normotensive and hypertensive patients, ambulatory blood pressure monitoring (ABPM) shows a higher degree of reproducibility with blood pressure readings taken in the clinical visits (Staessen et al., 2017). Patients who have white coat hypertension have elevated blood pressure when being measured in the doctor's office, but have normal blood pressure values during 24-hour ambulatory blood pressure monitoring (Mancia and Zanchetti, 1996). Therefore, clinic blood pressure readings may overestimate the patients' actual blood pressure levels (Flynn et al., 2017, Lurbe et al., 2016, Mancia et al., 2013). The European Society of Hypertension recommends the use of ABPM to screen patients with increased clinic blood pressure readings in order to avoid unnecessary antihypertensive treatment (Lurbe et al., 2016). Although it is widely accepted that patients that have white coat hypertension should not receive antihypertensive treatment, white coat hypertension was found to be a risk factor of cardiovascular disease (CVD) in both adults (Kuwajima et al., 1993, Nalbantgil et al., 1998) and adolescents (Vaindirlis et al., 2000).

Cuff size

Selection of an arm cuff of the correct size is necessary for accurate measurement of blood pressure. Using a cuff of incorrect size may lead to incorrect blood pressure readings. Blood pressure measurements are overestimated with a cuff that is too small and are underestimated by a cuff that is too large (NHBPEP-working-group, 2004). The mistakes in measurements can result in a fault in diagnosis and follow-up treatment of hypertension. This is of particular importance in children and adolescents, who have age-dependent variations in body size (Mattoo, 2002). According to *The Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents,* the recommendations of size of cuff relevant to different upper arm circumference are shown in Table 4.1 .

Table 4.1 cuff size and upper arm circumference

Arm band size	Upper arm circumference
Small	22cm and under
Normal	23cm – 34cm
Large	Over 34cm

4.1.2 Review of devices to measure blood pressure

Obtaining accurate and reliable blood pressure data is key for accurate diagnosis, management and academic research of hypertension. As high blood pressure is a chronic disease, self-measurement of blood pressure is an important way to supervise blood pressure for patients.

In clinical practice and research, several types of blood pressure monitors have been used. Each of them has its own advantages and disadvantages.

Auscultatory blood pressure monitors

Auscultatory blood pressure monitors, including mercury sphygmomanometers and non-mercury sphygmomanometers, are a type of traditional device for blood pressure measurement. They can provide accurate blood pressure value, and therefore have been used for many years, and have been recommended to be used as a standard device when validating other blood pressure monitors (O'Brien et al., 2010). However, the accuracy of the result is highly dependent on the operator. For example, the speed to deflate the bladder or the interpretation of the pulse wave will both affect the result (Francoeur, 2010). The measurement should be conducted by a trained observer, and should follow exactly the standard protocol (O'Brien et al., 2003). Meanwhile, mercury use is related to safety and environment issues, and therefore sphygmomanometers containing mercury have been recommended to be replaced in clinical practice(Committee of Blood Pressure Monitoring in Clinical Practice, 2005).

Electronic automated blood pressure monitor

The electronic automated blood pressure monitor is a popular alternative to auscultatory methods with several advantages. It is easily operated, allowing people, especially those without medical background, to measure their blood pressure themselves by simply fixing a cuff and pressing a button. Meanwhile, compared to auscultatory blood pressure monitor and Ambulatory blood pressure monitoring (ABPM), the automated

blood pressure monitors are affordable at a lower price. Medical institutions such as the Association for the Advancement of Medical Instrumentation, the European Society of Hypertension and the British Hypertension society have published standard protocols to validate automated blood pressure monitors (O'Brien et al., 2010, O'Brien et al., 1990, Association for the Advancement of Medical Instrumentation). According to those protocols, a large number of automated blood pressure monitors have been validated. In the United Kingdom, a list of validated blood pressure monitors by the British Hypertension Society can be found on their website (Burrows et al., 2015). Another list of recommended electronic blood pressure monitors was generated by O'Brien, based on the results from an investigation of the market for devices for blood pressure measurement in 2001 (O'Brien, 2001). Researchers have conducted validation of electronic automated blood pressure monitors in children and adolescents as well (Wong et al., 2006, Alpert, 2011, Alpert, 2007), several types of electronic blood pressure monitors have been proven to provide accurate blood pressure measurements in children and adolescents.

Smart phone applications

Nowadays, with the development of smart phone techniques, several applications provide a novel way to measure blood pressure. They can measure blood pressure by putting a finger on the screen or in front of the camera. It seems to be a convenient and easy way to operate. A large number of smart phone applications aimed to measure blood pressure without linked devices can be found in the application market, but the accuracy of those applications has seldom been investigated. During November 2014 to February 2015, a brief review and validation of existing applications was carried out (see results section) but the results did not support the usage of this method in monitoring of blood pressure in clinical practice and academic research.

Ambulatory blood pressure monitoring

Ambulatory Blood Pressure Monitoring is a method such that your blood pressure is being measured while living your normal daily life, for example moving around, eating, exercising or sleeping. A digital blood pressure machine will be attached to a belt around the body of the participant, and a cuff attached to the upper arm will be connected to the blood pressure monitor. The monitor takes blood pressure readings at regular intervals throughout the day over a period of 24 hours. Using ABPM provides

paediatricians with a more precise evaluation of a child's BP readings than office BP readings. It is the gold standard for diagnosing white coat hypertension (Krmar, 2018).

Other novel ways to obtain blood pressure data

Some novel ways to measure blood pressure have been reported, such as mobile phone based wireless blood pressure monitoring systems , which still relays on automatic blood pressure monitors, and cuff-less differential blood pressure estimation using smart phones (Woldendorp et al., 2014, Chandrasekaran et al., 2013, Wang et al., 2011). But these techniques are only in development and are not commercialized and therefore cannot currently be applied in clinical practice or academic research.

4.1.3 Background on Self-measured blood pressure

The accuracy of self-measured blood pressure in adults has been evaluated (Alonso et al., 2005, Centers for Disease and Prevention, 2002, Turiano et al., 2012), but relevant studies in adolescents are lacking. Meanwhile, there are special issues which should be taken into consideration when measuring blood pressure in adolescents. For example choosing the correct cuff size (Ostchega et al., 2014, Silva et al., 2014, Jenner et al., 1992, Whincup et al., 1989, Muhamed et al., 2016) and avoiding the white coat effects (Wang et al., 2017, Fujita et al., 2016). Therefore it is important to validate self-measurement of blood pressure in adolescents and not rely on data in adults.

Another way to obtain blood pressure in a community is to train agency social workers to conduct the measurements instead of physicians or researchers(Francoeur, 2010). This could be taken into consideration in the research design where frequently blood pressure monitoring is needed. This method was used in the UK National Diet and Nutrition Survey, including both adults and adolescents populations (England).

4.2 Aims

The aims of this study are:

a. to explore using smart phone applications to measure blood pressure values
b. to design a standard instruction leaflet and protocol for adolescents to measure their own blood pressure and validate its accuracy
c. to recommend an appropriate method and tools of blood pressure measurement to be used in an online health survey

4.3 Methods

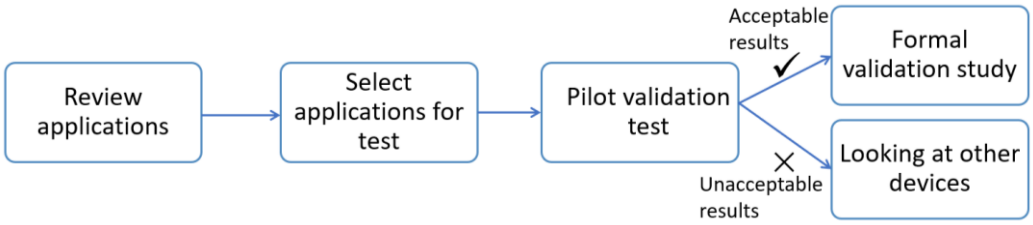
4.3.1 Exploration of smart phone applications to measure blood pressure

Study design

The study design is shown in Figure 4.1. Firstly, applications on the market were reviewed, and applications that met the criteria were selected to include in the pilot validation test. The pilot validation test was carried out with a small group of participants. Those applications that were found to provide precise and accurate blood pressure readings would be tested in a formal validation study in a larger sample.

The devices used in the study were the iPhone 4 (IOS) and Samsung (Android system) smartphone.

Figure 4.1 Study design of exploration of smart phone applications to measure blood pressure



Review of all smart phone applications in Apple app store and Google play

The Apple app store and Google play are the top two largest application stores in the world over the last 5 years (Master-of-Code-Global, 2017, The-Market-Mogul-Team, 2017). Each of them had nearly 1.5 million available applications at the end of 2014 (Master-of-Code-Global, 2017), and the numbers grew to 2.8 million in Google play and 2.2 million in the Apple app store in the year of 2017 (The-Market-Mogul-Team, 2017). The review of applications was carried out between November 2014 and February 2015 in these two application stores. A search was carried out with the key words ‘blood pressure’. In both of these two stores, applications designed for smartphones and tablets were all included, as some applications designed for tablets could also run on smart phones. The included applications were excluded by the researcher according to the following exclusion criteria:

a. Applications that aimed to explain knowledge on blood pressure health according to their description

b. Applications that aimed to record daily blood pressure rather than measuring blood pressure according to their description
c. Applications that claimed to be ‘fake blood pressure monitor’ ‘joke’ or ‘prank’ according to their description
d. Applications that did not met the first three criteria, but could not be downloaded or could not run on the smart phones.

Tests on the selected applications

The applications included in the review were downloaded to the devices. The pilot validation test was done with a small group of volunteer users within the department. The smart phone application validation study was to test usability and accuracy of each application. The protocol of the test was:

a. Each user sat still for about 15 minutes before taking the measurement.
b. The user started measuring their blood pressure using the smart phone applications. For each application, they were asked to take the measurement three times, with a 1 minute rest between each measurement. The researcher recorded the blood pressure values on the instruction after each measurement.
c. For each user, the researcher measured his/her upper arm circumference, chose the correct size of arm band and measured the blood pressure values using the validated blood pressure monitor (Omron 705IT) for a further three times to get the standard blood pressure values. The researcher recorded the blood pressure values after each measurement.

4.3.2 Validating the accuracy of self-measured blood pressure

Following the user testing of the smartphone apps we also decided to review electronic automated blood pressure monitors for use in the online survey.

Select blood pressure monitors

A brief review of previous studies on blood pressure monitors validation was carried out to select the blood pressure monitor to be used in the study. All brands and models of blood pressure monitors that is under 50 Pounds listed on the British Hypertension Society website(British_and_Irish_Hypertension_Society) were considered. Among them, the model which attaches cuff to the arm, and is available on the market with the lowest price was selected to be used in the study.

Ethical approval

Ethical approval for the validation of blood pressure self-measurement for adolescents was obtained from the Mathematics and Physical Science and Engineering joint Faculty Research Ethics Committee, University of Leeds (Reference Number is MEEC 15-030, Appendix 2). All of the participants were informed (Appendix 3) about the survey and gave consent before recruitment (Appendix 4). For adolescents aged under 16 years, both the adolescent's and their parent's (or guardian's) consent were obtained (Appendix 5). Consent of the headteacher was obtained in the local school where the study was carried out (Appendix 6).

Sample size calculation

In the validation of blood pressure self-measurement in adolescents, sample size was calculated based on the estimated sample size calculation for a paired-sample comparison of means, using Stata/SE 13.1 for Windows (64-bit x86-64). Means and standard deviations (SD) of blood pressure values of UK adolescents were obtained from the NDNS (2008-2012), which is a high quality and nationally representative dataset. The Mean±SD of systolic blood pressure was 111.97±10.71 mmHg, and the minimum sample size is 49. That of diastolic blood pressure was 63.20±8.53 mmHg, and the minimum sample size is 31. To make sure the sample size is enough to detect difference for both systolic and diastolic blood pressure values, the minimum sample size of the study is 49. It allows us to detect 5mmHg difference in both systolic blood pressure and diastolic blood pressure between the two methods at 90% power and alpha =0.05.

Sampling

In the validation of blood pressure self-measurement in adolescents, participants were recruited in 3 ways during October 2016 to March 2017, including University Open days, local school and first year students in the University.

University Open day

Participants were recruited on three of the University of Leeds open days (23/06/2016, 24/06/2016 and 10/09/2016) on campus, using convenience sampling method. On the open days, secondary school students who were about to graduate visited the University, most of them came with their parents. Stalls were set up in the School of Food Science and Nutrition. Posters (Appendix 7, in size A4) were displayed on the

stall. Flyers (Appendix 7, in size A5) were sent out to the visiting students. The students that were interested in the study received detailed information sheets (Appendix 3). The parents of those under 16 years old received the information sheets as well. Students agreed to take part in the study signed the consent form (Appendix 4) before being enrolled. The parents of those under 16 years old signed the consent form (Appendix 5) as well. The study was carried out in the common room of the department.

Local school

Lists of secondary schools in Leeds and Wakefield were obtained from the Leeds City Council website (Leeds-Council) and Wakefield City Council website (Wakefield-Council) in March 2016. 40 schools were included in Leeds, and 23 in Wakefield. Contact information of the schools (email addresses and telephone numbers of the headteachers/receptions) were found on the official websites of each school. Recruiting emails were sent to all the secondary schools in Leeds and Wakefield on that list, and follow-up phone calls were made to the schools to ask if they had an interest in taking part in the research study (Appendix 8).

The study was carried out in an A-level club in Roundhay secondary School. We had a recruiting session on 12/10/2016, where we introduced the study to the students (all over 16 years old), 16 of them signed a consent form after the session on that day. We had two following interview sessions on 19/10/2016 and 23/11/2016. 19 students who are interested in the study were recruited (12 on 19/10/2016 and 7 on 23/11/2016), among them, all of those who did not attend the recruiting session were given information sheets and signed consent forms. The study was carried out in a classroom of Roundhay School.

First year students of the University of Leeds

In addition to the local school recruitments, during October 2016 to March 2017, we sent emails to the Student Education Service Officers and/or School Education Support Officers in all the 20 schools in the University of Leeds, asking them to help us distribute recruiting emails around their first year students. Among all the schools, 7 schools responded to the requesting email, and helped to promote the study. They were School of Food Science and Nutrition, School of Chemistry, School of Maths, School of Physics, School of Mechanical Engineering, School of Geography and School of Environment. Twenty nine first year students were recruited in this way. We booked a

date and time for interview for each participant through email. The study was carried out in the Group Study Rooms in the Laidlaw Library.

Data collection

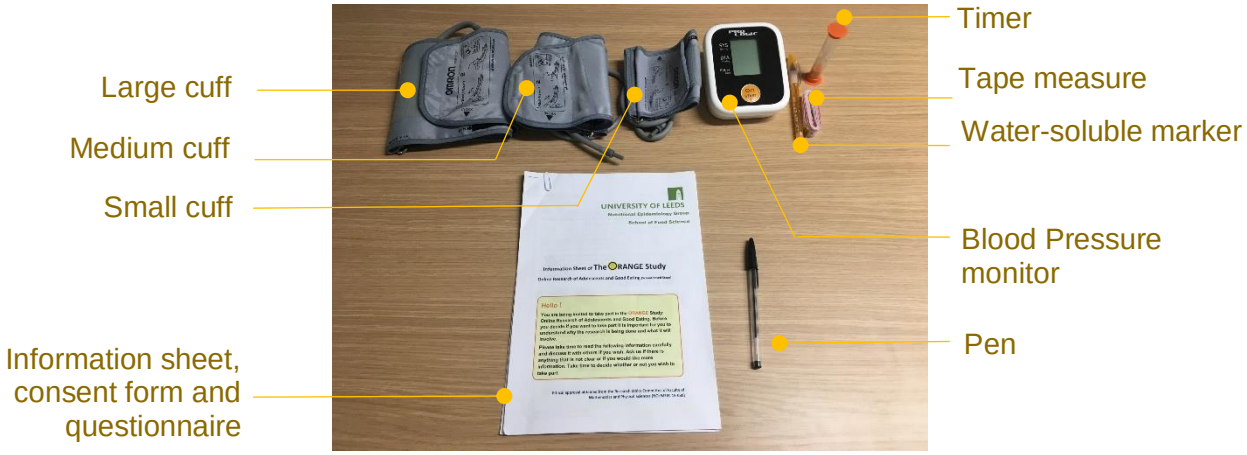
Design of blood pressure monitor instructions (Appendix 9)

Although lots of instructions on how to measure blood pressure can be found online, we designed an easy-to-read instruction leaflet for the participants. The self-designed instruction leaflet was based on the standard protocol of blood pressure measurement and emphasized important points such as don't eat, drink, talk or move during the measurements, and sit still between measurements for participants carrying out the measurements for themselves. It had a colourful page layout, included lots of pictures and fewer terms, which were more acceptable for adolescents. It also had a detailed description of how to measure upper arm circumference and choose the correct cuff size, which are particularly important for adolescents, who have a more variable upper arm circumference than adults. Before using it in the formal study, the instruction was evaluated by three adolescents in a small pilot study. Feedback was collected from the pilot participants, and included suggestions such as reducing the use of terms, replacing some text with pictures and providing a more colorful design.

Protocol of measurements

a. The participant was given the information sheet and signed the consent form if they agreed to take part in the study. For participants under 16 years, their parents also received the information sheet and signed the consent form.
b. After giving consent, the participant was asked to remove their coat or jumper that covered their upper arm. The participants received a pack of tools to measure blood pressure, including the instruction, a blood pressure monitor (Omron PL100), three cuffs in small/median/large size, a tape measure, a timer, a water-soluble marker and a pen. See Figure 4.2.

Figure 4.2 Tools to measure blood pressure



c. Each participant sat still for about 15 minutes before taking the measurement. In this study, the participants were doing a questionnaire during that time.

d. The participant read the instructions, familiarized themselves with all the tools, and then started the measurement by measuring their upper arm circumference, and choosing a correct cuff based on the result.

e. The participant started measuring their own blood pressure. In the instructions, they were asked to take the measurement three times, with 1 minute between each measurement. The participant wrote the blood pressure values on the instruction after each measurement. See Figure 4.3.

Figure 4.3 Participants measuring their own blood pressure

f. After the self-measurement, the researcher measured the participant's upper arm circumference, chose the correct arm band and measured the blood

pressure using the same blood pressure monitor for a further 3 times to get the standard blood pressure values. The researcher recorded the blood pressure values after each measurement.

Data cleaning

Excluding outliers for each participant

For each participant, outlier values were identified using the following method, taking SBP as an example, SD of the 3 SBP values were calculated for every participant. An outlier SBP value was identified if SD>20 mmHg, and then the outlier was excluded from the 3 SBP values. The same method was used to exclude outlier values for DBP, where the cut off point for SD was 16 mmHg.

Calculation of mean blood pressure values

Mean blood pressure values were calculated based on the second and third measurement. If one of them was an outlier value and had been excluded, the remaining value was used.

Exclusion of outliers

The participants might make movements after measuring their own blood pressure and before the researcher measures their blood pressure, which might cause variation in self-measured blood pressure values and standard blood pressure values. Differences of self-measured and standard blood pressure values were calculated. Mean and SD of differences were calculated. Those cases that had differences larger than mean±2*SD were defined as outliers.

Statistical analysis

Distributions of age, gender and how the participants were recruited were described using percentages. Three methods were used to evaluate the accuracy of self-measured blood pressure values: a) a paired t-test was conducted to detect the difference of self-measured and standard blood pressure values. b) percentage of difference values larger than 5mmHg were calculated, and c) A Bland- Altman plot was generated to investigate the agreement of self-measurements and standard measurements.All statistical analyses were carried out using Stata/SE 13.1 for Windows (64-bit x86-64). Alpha =0.05.

4.3.3 Comparison and selection of methods to use in the online survey

After testing smart phone applications and the self-measurement using automatic blood pressure monitor, a method will be selected to be used in the online survey. Taking the expenditure and feasibility into consideration, the following four criteria should be considered when selecting the blood pressure monitor:

a. highly accessible at home or easy to post
b. low price
c. easy to operate
d. high reliability and validity of results.

4.4 Results

4.4.1 Exploration of smart phone applications to measure blood pressure

500 results in iTunes and 250 in Googleplay were found. After reviewing all of them, 1 app in iTunes and 3 apps in Googleplay were identified as designed to measure blood pressure using a smart phone.

Four test users were recruited in the School of Food Science and Nutrition. Their blood pressure was measured using all the apps and a validated standard blood pressure monitor, three times each. The results are displayed in Table 4.2. Compared to the results from the standard blood pressure monitor, the results from apps all ranged widely, and the standard deviations were quite large, which means that none of those applications were able to provide reliable and valid blood pressure values. In conclusion, all of the four apps were ineligible to use in clinic or research settings. Therefore, no further validation studies on blood pressure measuring applications was carried out.

Table 4.2 Results of validation of smart phone applications

Device	User 1		User 2		User 3		User 4	
	Three measurements	Mean (SD) Difference with validated	Three measurements	Mean (SD) Difference	Three measurements	Mean (SD) Difference	Three measurements	Mean (SD) Difference
Lloyds BP monitor (Validated)	109/61	106.33(3.06)/ 64.00(4.36)	140/73	134.33(7.37)/70.67(3. 21)	113/74	115.00(3.46)/78.33(3. 79)	136/91	134.00(2.65)/92.3 3(1.53)
	103/69		137/72		119/80		135/94	
	107/62		126/67		113/81		131/92	
Blood Pressure Checker (Android)	160/93	139.67(27.79)/84.00(8.54)	126/91	137.00(12.77)/92.00(9.54)	102/84	122.33(27.79)/83.00(1.73)	111/78	126.33(13.87)/93. 00(13.23)
	108/76	33.34/20.00	134/102	2.67/21.24	111/81	7.33/4.67	130/98	-11.45/0.67
	151/83		151/83		154/84		138/103	
BloodPressure Cal (Android)	122/83	122.00(7.00)/84.00(1. 00)	109/66	119.67(11.02)/75.00(8.54)	109/66	116.67(10.79)/78.00(10.44)	128/88	133.00(8.66)/91.3 3(5.77)
	115/84	15.67/20.00	131/83	-14.66/4.33	112/83	1.67/-0.33	128/88	-1.00/-1.00
	129/85		119/76		129/85		143/98	
Finger Print Blood Pressure Meter (Android)	153/77	162.33(8.62)/72.00(8. 66)	131/63	141.67(24.79)/73.33(10.02)	127/82	123.00(6.93)/89.33(8. 74)	176/72	169.33(12.42)/76. 33(10.21)
	164/77	56.00/8.00	170/83	7.34/2.57	127/99	8.00/11.00	155/88	35.33/-16.00
	170/62		124/74		115/87		177/69	

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Real Blood Pressure (BP) Calculator (Android)	115/75	115.67(5.03)/75.33(4.51)	118/77	120.00(5.29)/78.00(3.61)	133/88	131.67(5.13)/86.33(3.79)	149/97	142.00(13.00)/92.00(9.54)
	121/80	9.34/11.33	116/75	-14.33/1.33	126/82	16.67/8.00	150/98	8.00/-0.33
	111/71		126/82		136/89		127/81	
BP Measure (Apple)	100/67	98.00(2.00)/65.00(2.00)	96/63	97.00(1.00)/63.67(1.15)	103/66	105.67(2.52)/68.33(2.52)	103/68	103.00(1.00)/68.67(1.15)
	96/63	-8.33/1.00	98/65	-37.33/-7.00	108/71	-9.33/-10.00	102/68	-31.00/-23.66
	98/65		97/63		106/68		104/70	

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4.4.2 Validation of blood pressure self-measurement

Selection of blood pressure monitors

Sixteen blood pressure monitors were listed on the British Hypertension Society website (British_and_Irish_Hypertension_Society), which attach cuffs to the arm and under 50 pounds were considered. Among them, the model which is available on the market with the lowest price was Omron PL100. The price of it ranged from 16 pounds to 21 pounds. This blood pressure monitor was selected to be used in the study.

General information

The Roundhay School in Leeds agreed to take part in the study. The headteacher signed the consent form for schools (Appendix 6). The school is located in north Leeds and has a mixed intake of students from a range of socio-economic backgrounds.

The total sample size was 53. Four SBP values and five DBP values were excluded. Two participants were excluded because they were defined as outliers, leaving a valid sample size of 51. This is larger than the minimum sample size (49) planned. There were 20 (38%) boys and 33 (62%) girls. the majority of them were 18 or 19 years old. See Table 4.3.

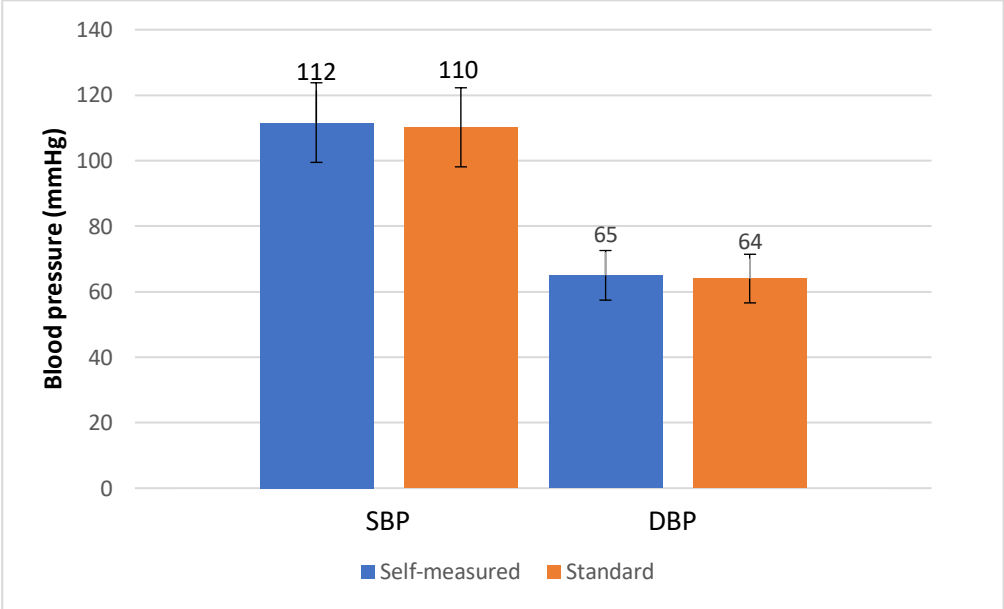
Table 4.3 General Information

Item	N (%)
Gender	
Male	20 (38%)
Female	33 (62%)
Age (years)	
14	1 (2%)
16	7 (13%)
17	13 (25%)
18	16 (30%)
19	16 (30%)
Recruited from:	
Open Day	5 (9%)
Local School	19 (36%)
1st year students in the University of Leeds	29 (55%)

Difference between self-measured and standard BP

The mean self-measured SBP was 112.4±12.2 mmHg, the mean standard SBP was 111.1±12.0 mmHg, and the mean difference was 2.6 mmHg. The mean self-measured DBP was 65.5+ 7.6 mmHg, the mean standard DBP was 64.5+7.4 mmHg, and the mean difference was 1.1 mmHg. No significant difference was found between self-measured and standard SBP or DBP (p value= 0.241 for SBP, 0.053 for DBP). See Figure 4.4.

Figure 4.4 Comparison of self-measured and standard SBP/DBP in adolescents



Difference between self-measured and standard blood pressure values

Twenty two (43%) out of the 51 self-measured SBP values had a difference larger than 5 mmHg compared to standard SBP values, and 10 (20%) out of the 51 self-measured DBP values had a difference larger than 5 mmHg compared to standard DBP values.

Measures of agreement

In the Bland- Altman Plot, 1 outlier SBP difference value and 3 outlier DBP values were found. 98% of SBP difference values and 96% DBP difference values were within the 95% confidence interval, which shows an acceptable agreement between self-measured and standard blood pressure values. See Figure 4.5 and Figure 4.6.

Figure 4.5 Bland-Altman plot of systolic blood pressure

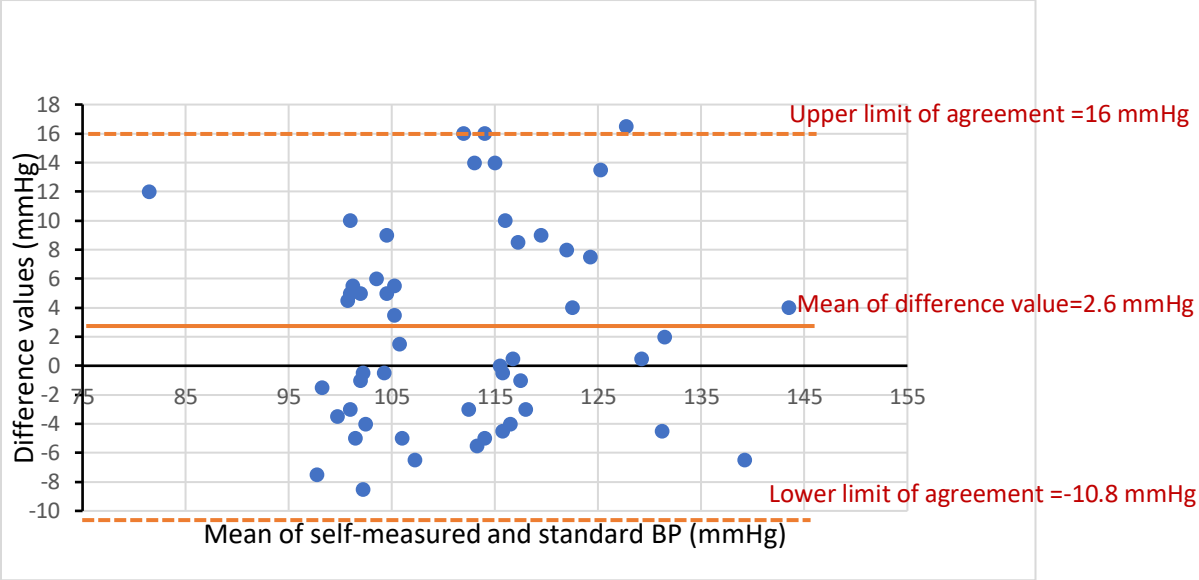
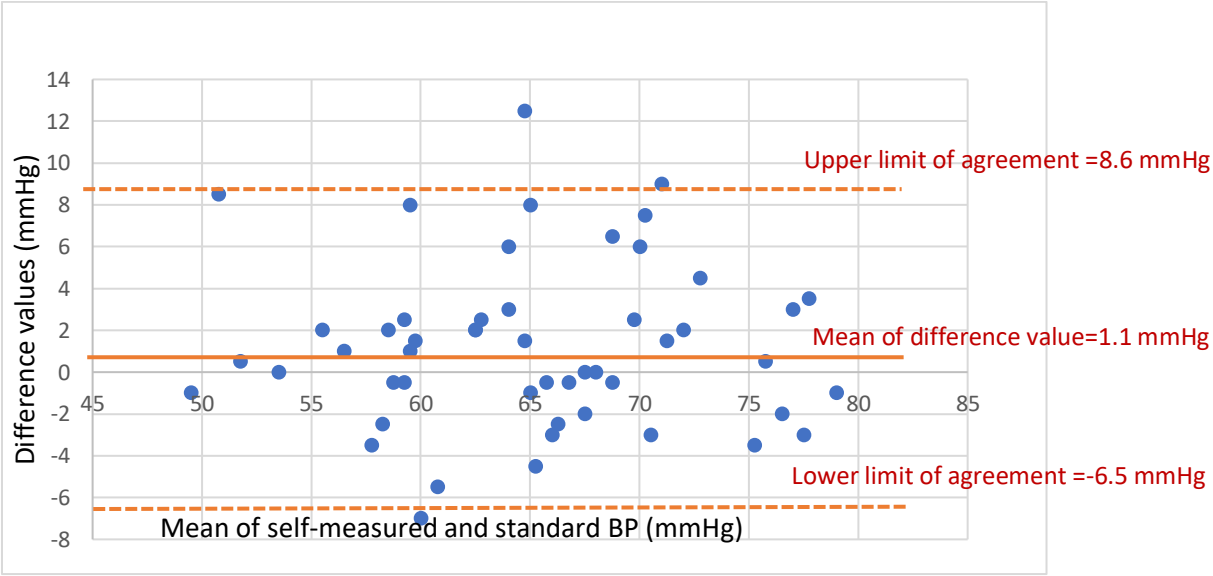


Figure 4.6 Bland-Altman plot of diastolic blood pressure



4.4.3 Selection of method to use in the online survey

A summary of different types of blood pressure monitors is provided in Table 4.4. According to information shown in Table 4.4, automated blood pressure monitor (Omron PL100) is accessible by post, low price, easy to operate. Combining with the use of our self-designed instruction, adolescents can provide reliable readings in self-measurements. Therefore, Omron PL100 combined with the self-designed instructions were selected for use in the online survey.

Table 4.4 Summary of blood pressure measuring devices and methods

Devices/Method	Accessibility (Home/Post)	Low price	Easily operate	Reliable result
Auscultatory BP monitor	X	X	X	√
ABPM	X	X	X	√
Automated BP monitor				
-wrist	√	√	√	X
-upper arm (self-measured)	√	√	√	√
Smart phone apps	√	√	√	X

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4.5 Discussion

4.5.1 Summary of the results

In the current study, Omron PL100 blood pressure monitor combined with the self-designed instructions were selected to use in the online survey for the participants to measure their own blood pressure. Auscultatory BP monitor and ABPM can provide accurate results but are not commonly used at home and not easy to send by post. Also ABPM is a high price which makes it unfeasible to use in a large-scale epidemiology study. The smart phone applications are free and easy to download for the participants, but none of the applications tested could provide reliable and valid blood pressure readings. Using Omron PL100 and the self-designed instructions, the adolescent's self-measured blood pressure and standard blood pressure values did not have statistically significant differences and blood pressure values from two methods showed acceptable agreement in a Bland-Altman Plot. The results support the accuracy of self-measured blood pressure values in adolescents.

4.5.2 Validation of smart phone applications that can measure blood pressure

According to the results from the pilot study, none of the tested smart phone applications can provide blood pressure readings with appropriate accuracy. The blood pressure values from the applications had either wide variance or big differences compared with the standard blood pressure values. No further large-scale validation was carried out, for the sake of saving expenditure and time. All these applications measure blood pressure by letting the participants put their finger on the screen for several seconds, and then providing the blood pressure readings. It seemed that this method is not reliable because not all smart phones have a pressure sensor on their screens.

There are a lot of smart phone applications that can be linked with a wireless blood pressure monitor and record the blood pressure values. But applications that can measure blood pressure by themselves are not common. Therefore, research testing the accuracy of this kind of applications are few. In the year of 2014 and 2015 when the study was being undertaken, no similar studies could be found. However, in recent years there are a few studies that have tested the accuracy of smart phone applications claiming to measure blood pressure. In 2017, a study tested other four smart phone applications in healthy people, and reported a similar result to this pilot study

(Alexander et al., 2017). All of the four applications did not provide clinically meaningful data. In 2018, a new application, Preventicus BP smartphone algorithm was developed and tested on 32 pregnant women by Raichle (Raichle et al., 2018). According to the requirement of European Society of Hypertension International Protocol revision 2010, the application failed the standards for accuracy for measuring blood pressure in the pregnant women. On the other hand, some studies found promising methods to measure blood pressure only using smart phones (Matsumura et al., 2018, Chandrasekhar et al., 2018, Chandrasekaran et al., 2013). Chandrasekhar (Chandrasekaran et al., 2013) and Matsumura (Matsumura et al., 2018) developed similar methods (Oscillometric Finger Pressing Method) to estimate blood pressure levels with reasonable accuracy by calculating blood pressure values using heart rate and modified normalized pulse volume. These two figures can be measured using smartphone and its built-in camera. In 2018, Chandrasekhar (Chandrasekhar et al., 2018) developed an iPhone X application to measure blood pressure values using this method, and tested the application in 22 healthy participants. The results indicated that the application can provide relatively accurate blood pressure readings, and may be feasible to use in many existing smart phones. Compared to the finger-cuff blood pressure monitor, which was used as a standard device, the application showed errors that were only about 2 mmHg higher on mean. However, there are some shortcomings made and the results of this study are not robust. The finger-cuff blood pressure monitor was not validated by any international academic association, which means their 'standard blood pressure values' might be biased. The application was only tested in healthy participants, but not in hypertensive participants. Its ability to provide accurate blood pressure readings in a higher range was not tested. Also the sample size was quite small, which made the study less powerful.

4.5.3 Validation of blood pressure self-measurement

Before analysis, the raw data was cleaned using the methods mentioned previously. Firstly, outlier blood pressure values of each participant were excluded. Secondly, outlier cases were excluded.

For each participant, outlier SBP/DBP values were excluded. This was because the outlier values might reflect incorrect behaviour during the self-measurement or during the standard measurement. The participants were asked to measure their own blood pressure three times, and had their blood pressure measured by the researcher for a

further three times. Although the participants were asked to sit still, they might still talk or make movements, which would influence (normally increase) their blood pressure values. In this situation, an outlier blood pressure value which was far from the other two values would be generated. These outlier blood pressure values did not represent the participants' true blood pressure levels when they were supposed to sit still. The cut-off point for SD equalled to the Mean SD + 2 (SD of all SD), which ensured a sufficient sample size.

Outlier cases were defined as those that had large differences between standard blood pressure values and self-measured blood pressure values. The large difference might reflect incorrect behaviour between self-measurement and standard measurement which might influence the participants' blood pressure levels. The cut-off point for differences equalled to the Mean Difference + 2 (SD of differences). Reducing the cut-off point can increase the accuracy, but it will also reduce the sample size. The current cut-off point ensured a sufficient sample size (49).

In the online study, the outlier SBP/DBP values should be excluded using the same method, to ensure the accuracy of self-measured blood pressure values.

The results were acceptable at the population level, while at the individual level, the results are less reliable. More participants obtained self-measured BP values that had a large difference (larger than 5 mmHg) from standard values in SBP than in DBP. Twenty two (43%) out of the 51 self-measured SBP values had a difference larger than 5 mmHg compared to standard SBP values, and 10 (20%) out of the 51 self-measured DBP values had a difference larger than 5 mmHg compared to standard DBP values. The results in individuals indicates that when analysing self-measured blood pressure data in the future online survey, the results involving DBP are anticipated to be more reliable than those involving SBP.

4.5.4 Strengths and Limitations

The current study provided evidence on self-measurements of blood pressure in UK adolescents. Using the tested blood pressure monitor (Omron PL100) and the self-designed instruction, adolescents can easily measure their own blood pressure values and be aware of their blood pressure status, which could benefit not only in health research, but also household blood pressure monitoring in adolescents. As hypertension was more common in adults, household blood pressure monitor was wider studied and

used in adults. Adolescents commonly do not have their blood pressure measured, which may be linked with unrevealed hypertension. Hypertensive adolescents more commonly have their blood pressure measured in the clinics. Restricting measurements of blood pressure to the clinics could link with biased blood pressure readings because of the white coat effect. It may also worsen the daily blood pressure monitor for hypertensive adolescents.

The validation of smart phone applications was only carried out in a pilot study with 4 participants, no large-scale study was done. This was because the current results did not indicate that a promising application can be found to provide accurate blood pressure readings.

In the validation of blood pressure self-measurement, most of the participants were over 16 years old. Because of hard of access, results of younger adolescent are lacking. Therefore the results cannot be generalizable to younger aged adolescents.

4.5.5 Perspectives

It is necessary to develop reliable portable blood pressure monitoring devises, for example smart phone applications or blood pressure monitors in a smaller size. The use of Oscillometric Finger Pressing Method is promising, but the relevant smart phone application should be validated in a large population, which should include hypertensive participants.

Further studies on developing different methods to measure blood pressure in adolescents, especially in younger adolescents are needed to improve the research and management of hypertension in adolescents. The method we developed (Omron PL100 plus self-designed instruction) should be tested in younger adolescents.

4.6 Conclusion

In a small-scale pilot study, five smart phone applications claiming to measure blood pressure were tested, and none of them were found to provide accurate blood pressure readings. However, following our self-designed instruction and using the validated blood pressure monitor (Omron PL100), adolescents could measure their own blood pressure and provide blood pressure readings that had acceptable agreement with standard blood pressure values.

The combination of Omron PL100 blood pressure monitor and our self-designed instructions were selected to be used in the future online survey. The tools are low cost, easy to operate and are possible to post to the teenage participants in the future online survey.

Chapter 5. A pilot study using new technology in an online epidemiological survey

Abstract

Background: Carrying out epidemiology research online rather than using traditional face-to-face methods is becoming a novel method worth studying. These new methods will allow researchers to obtain sample in a wider geographic area with lower costs in time and money, are more convenient and are more acceptable for participants to collect sensitive information. The aim of the study is to explore the feasibility of use new technology in epidemiology studies.

Methods: The Online Research of Adolescents and Good Eating Study (ORANGE Study) was set up to explore the feasibility of online survey. It included two stages:

School-based stage: participants were recruited from local school students, visiting students on university open-days and first year students in the University of Leeds. Questionnaires were used to find out the adolescents' Internet habits and attitude to an online health research.

Web-based stage: participants were recruited through social network websites. A sub-sample were randomly selected to complete the whole study. They received blood pressure measuring tools by post, and were asked to measure their own blood pressure, complete an online questionnaire and a 3-day online dietary record. Response rates, completion rates, time and money expenditure and sample characters were calculated and compared to those of the school-based stage to evaluate the feasibility of online survey.

Results and conclusion: In the ORANGE study, 21% of the participants would like to click on the advert of online survey, and 32% of the participants would like to take part in the survey. In the pilot online study, response rate of the web-based sample was a bit higher than school-based stage. The web-based study expensed more money but less time. Compared with national data (NDNS population), in both school-based stage and web-based stage, fewer participants under 16 years were recruited, fewer male participants were recruited, and more white participants were recruited. There were significant differences between the online sample and the NDNS adolescent population in dietary intake of energy, total fat, carbohydrates, sugars, sodium and vegetables. No difference was found in either SBP or DBP.

5.1 Introduction

In recent years, carrying out health research online rather than using traditional face-to-face methods is becoming a novel method worth studying (Fenner et al., 2012, Gunasekaran et al., 2013), Recruiting and collecting data can all be done using Internet technologies.

One method to recruit participants online is through social networking websites, such as Facebook, Instagram, etc. (Fenner et al., 2012, Gunasekaran et al., 2013, Miyagi et al., 2014). This method saves time and/or money for the researcher, allows researchers to obtain sample in a wider geographic area and allows them to access the sensitive population more easily.

Today, online survey services and websites (for example, Bristol Online Survey, Qualtrics, Surveymonkey, etc.) make online research much easier, the researchers do not need to learn complicated Internet technologies such as HTML coding and scripting programs(Wright, 2005). It is also less time consuming for the participants to compete the questionnaire whenever and wherever they like, using PC, lab top or even mobile phones. Data on these websites can be easily obtained by the researchers, at the same time, the data is safe-guarded. Myfood24 is a website designed to collect diet data online. Nutrition information of common foods in the UK is included in its database. Participants can access to the website and record their diet easily. This online diet record tool had been validated in UK adolescents (11 - 18 years) and adults (19 – 64 years) (Carter et al., 2015).

A recent report indicated that the majority of adolescents use the Internet everyday (Fenner et al., 2012, Gross, 2004, Gu et al., 2016, Madden et al., 2013). Thus evidence suggests that recruiting adolescents and carrying out a health survey through the Internet is possible and could be effective.

5.2 Aims

Part A (survey of adolescents' attitudes on an online health research): to investigate adolescents' attitudes on online health survey by face-to-face questionnaire, and design the protocol of pilot survey (Part B) based on the results.

Part B (pilot online survey): to test the feasibility, explore the advantages and disadvantages of online research by carrying out a pilot online survey.

5.3 Methods

5.3.1 Ethical approval

Ethical approvals for the ORANGE Study (Part A and Part B) were obtained from the Mathematics and Physical Science and Engineering joint Faculty Research Ethics Committee, University of Leeds (Reference Number were MEEC 15-030, Appendix 2, MEEC 16-002, Appendix 10). All of the participants were informed (Appendix 3 for school-based stage, Appendix 11 for web-based stage) about the survey and gave consent before recruitment (Appendix 4 for school-based stage, Appendix 12 for web-based stage). For adolescents aged under 16 years, both the adolescent's and their parent's (or guardian's) consent were obtained (Appendix 5 for school-based stage, Appendix 13 for web-based stage). Consent of the headteacher was obtained in the local school where the study was carried out (Appendix 6).

5.3.2 Part A: A survey of adolescents' attitudes on an online health research (school-based stage)

Sampling

Participants were recruited in 4 ways during October 2016 to March 2017, including University Open days, Summer school, local school and first year students in the University.

University Open day

Participants were recruited on three of the University of Leeds open days (23/06/2016, 24/06/2016 and 10/09/2016) on campus, using a convenience sampling method. On the open days, secondary school students who were about to graduate visited the University and most of them came with their parents. Stalls were set up in the School of Food Science and Nutrition, The Laidlaw Library and the Brotherton Library in the University of Leeds. Posters (Appendix 7, in size A4) were displayed on the stalls. Flyers (Appendix 7, in size A5) were sent out to the visiting students. The students that were interested in the study received detailed information sheets (Appendix 3). The parents of those under 16 years old received the information sheets as well. Students agreed to take part in the study signed the consent form (Appendix 4) before being enrolled. The parents of those under 16 years old signed the consent form (Appendix 5) as well. The study was carried out in the common room of the department.

Summer school

The School of Food Science and Nutrition held a summer school in July 2016, where the PhD researcher was allowed to enter one of the classes and briefly explained the study to the students. Students who were interested in the study signed the consent forms and were enrolled into the study on that class. The participants completed the questionnaire on that day.

Local schools in Leeds

Lists of secondary schools in Leeds and Wakefield were obtained from the Leeds City Council website (Leeds-Council) and Wakefield City Council website (Wakefield-Council) in March 2016. 40 schools were included in Leeds, and 23 in Wakefield. Contact information of the schools (email addresses and telephone numbers of the headteachers/reception staff) were found on the official websites of each school. Recruiting emails were sent to all the secondary schools in Leeds and Wakefield on that list, and follow-up phone calls were made to the schools to ask if they had an interest in taking part in the research study (Appendix 8).

The study was carried out in an A-level club in Roundhay secondary School. We had a recruiting session on 12/10/2016, where we introduced the study to the students (all over 16 years old), 16 of them signed a consent form after the session on that day. We had two following interview sessions on 19/10/2016 and 23/11/2016. 19 students who are interested in the study were recruited (12 on 19/10/2016 and 7 on 23/11/2016), among them, all of those who did not attend the recruiting session were given information sheets and signed consent forms. The study was carried out in a classroom of Roundhay School.

First year students of the University of Leeds

In addition to the local school recruitments, during October 2016 to March 2017, we sent emails to the Student Education Service Officers and/or School Education Support Officers in all the 20 schools in the University of Leeds, asking them to help us distribute recruiting emails around their first year students. Among all the schools, 7 schools responded to the requesting email, and helped to promote the study. They were School of Food Science and Nutrition, School of Chemistry, School of Maths, School of Physics, School of Mechanical Engineering, School of Geography and School of Environment. Twenty nine first year students were recruited in this way. We booked a

date and time for interview for each participant through email. The study was carried out in the Group Study Rooms in the Laidlaw Library.

Data collection

The questionnaire (Appendix 14) was designed by the researcher. It was composed of three parts: 1) general information (gender, age), 2) daily habits of using social networking websites and 3) attitudes to an online survey. Participants were asked to imagine seeing an advert about an online health survey when using Facebook or other websites. That survey was comprised of three parts: an online questionnaire, a 3-day dietary record and self-measurement of blood pressure. Then they were asked these three questions to measure their willingness to attend the survey: *Would you be interested and click on the ad? Would you like to take part in the survey? Would you like to tell your friends about the survey?* They were also asked how willingly they would like to complete each part of the survey. The participants were asked to rank factors that would affect their attitudes. The questionnaire was revised after being used on the first open day according to feedbacks from the participants. The updated version was used in all the following sessions.

Data analysis

Data from the questionnaires was entered and analysed using Microsoft Excel. Bar chart was used to display the single choice and multiple choices questions. For ranking questions, mean rank of each choice was calculated. Answers of text questions were categorized using key words, and then displayed using a frequency table.

5.3.3 Part B: A pilot online survey (web-based stage)

Online recruitment

Participants were recruited through Facebook and Instagram advertising. A website of the study was built to explain the details of the study (Appendix 15). A Facebook account of the study was registered to publish adverts. 6 rounds of advertising were carried out, using different strategies (Appendix 16).

Data collection of the pilot survey

The complete survey (includes blood pressure measurement, online questionnaire and online diet record) was carried out in a sub-group of participants that were randomly selected from the total sample, according to the following protocol:

Confirming postal address: an email was sent to the participants to confirm their postal address. Only those who replied and confirmed their address were enrolled into the further survey. For the first nine participants, we did not send an email to confirm the address, and it turned out the reply rate was low. Therefore this step was added in subsequent participants.

Posting tools: After getting the confirmation of their address, the tools were posted to the participants. The parcel included: 1 blood pressure monitor (with box, a normal size arm band in the box), 4 batteries (taken out to avoid the monitor to be turned on in transit), 1 timer, 1 tape measure, 1 black ball-point pen, 1 water-erasable pen, paper-works (To-do list, Instruction, Feedback Form, Return Checklist), a pre-paid return envelope. An email informing the parcel was on the way was sent to the participants right after the parcel was posted. An email informing what to do after receiving the parcel was sent to the participants on the next day.

Participants complete survey: the participants followed the instructions to complete the online questionnaire and complete blood pressure self-measurement. A 3-day online dietary record would start from the day they completed the questionnaire. An email from myfood24 website was sent to the participants each day, including the link to do an online dietary record. Reminder emails would be sent to the participants on the third, seventh, tenth day if they have not submit the diet record. The participants would post the tools back using the pre-paid return bag.

Receiving return parcel: an email was sent to the participants when their return parcel arrived to the researcher. The researcher checked the tools, the online questionnaire and dietary record. A gift voucher was sent to the participants who returned the tools.

Data analysis

The following data was analysed:

A comparison of response rates of the school-based stage and web-based stage was carried out. The valid response rate is defined as the percentage of participants who completed all parts of the survey. Response rates in each part of the survey were calculated and completed as well.

Comparison of time and money expenditures (total, per participant) of school-based stage and web-based stage were made.

Comparisons of demographic information of School-based sample, online sample and national data (NDNS adolescent population) were made.

Comparisons of dietary data and blood pressure levels of online sample and national data (NDNS adolescent population) were made, using t-tests.

5.4 Results

5.4.1 Part A: School-based study

General information

209 participants were recruited in total. From them 129 were recruited on open days (on 23/06/2016, 24/06/2016, 09/09/2016 and 08/10/2016), 36 were recruited in the summer school (in July 2016), 19 recruited in Roundhay School (on 19/10/2016 and 23/11/2016), and 25 recruited in 1st year students in University of Leeds (from October to December 2016). 114 (55%) were female and 95 (45%) were male. Most of the sample were 17 years old. (Table 5.1)

Table 5.1 General information

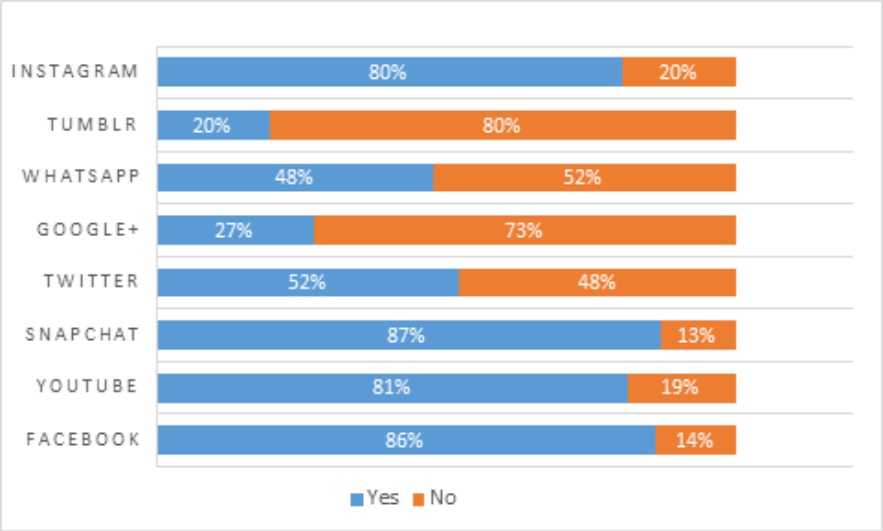
Item	N	%
Gender		
Female	114	55%
Male	95	45%
Age		
14	3	1%
16	23	11%
17	138	66%
18	32	15%
19	13	6%

Internet habits

Almost all of the participants (99%) had daily access to a computer, and all of the participants had a smartphone. Figure 5.1 shows how many of the participants use the listed social networking websites/apps at least once a week. In the figure, the most

popular websites/apps were Facebook, Youtube and Snapchat. Other websites/apps mentioned by the participants were Pinterest, buzzfeed and reddit.

Figure 5.1 Use of popular social networking websites/apps in adolescents



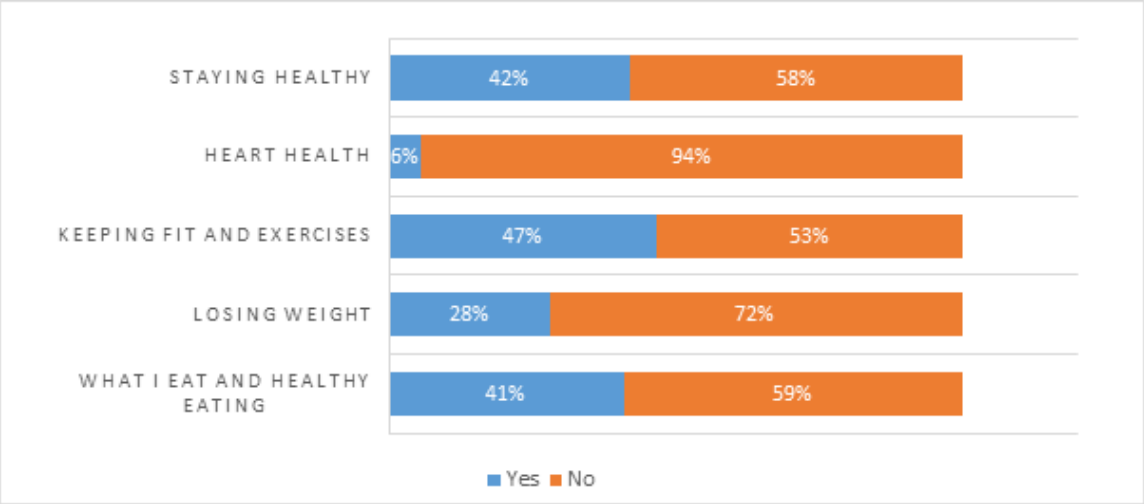
95% of the samples had a Facebook account, and 89% of the samples had used Facebook in the last week. The time adolescents spent on using Facebook is displayed in Table 5.2. More than half (54%) of the samples reported spending more than 30 minutes on using Facebook.

Table 5.2 Time adolescents spent on using Facebook

Duration	N	%
<=30 minutes	85	41%
0.5-1 hour, including 1hour	63	30%
1-2 hours, including 2 hours	30	14%
> 2 hours	20	10%
Not sure	11	3%

Figure 5.2 shows how many participants were interested in the listed topics related to health and nutrition when using internet. 45% of the participants were interested in *Keeping fit and exercise*, the other two popular topics were *What I eat & healthy eating* (35%) and *Staying healthy* (33%). Twenty percent of the participants were interested in the topic of *Losing weight*, while only 4% of the participants were interested in the topic of *Heart health*. 39% of them were interested in none of these above topics.

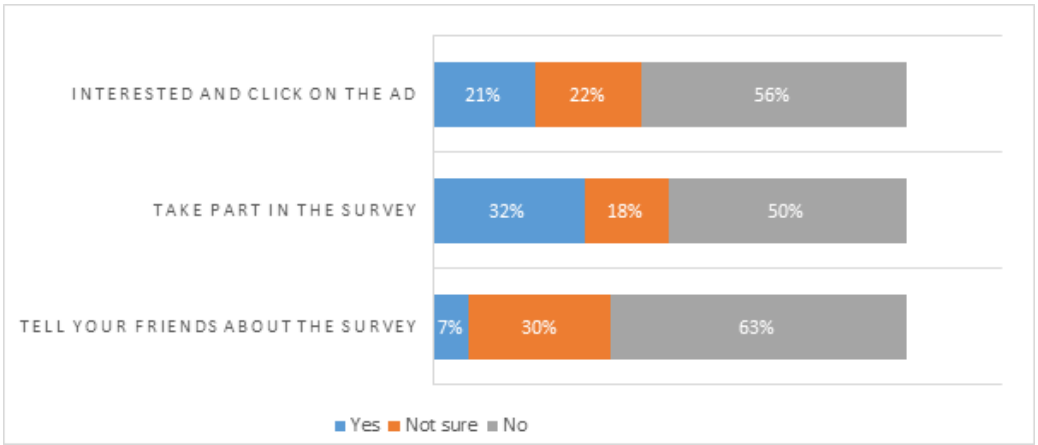
Figure 5.2 Adolescents' interests on health related topics when using the internet



Adolescents' attitudes to an online health survey

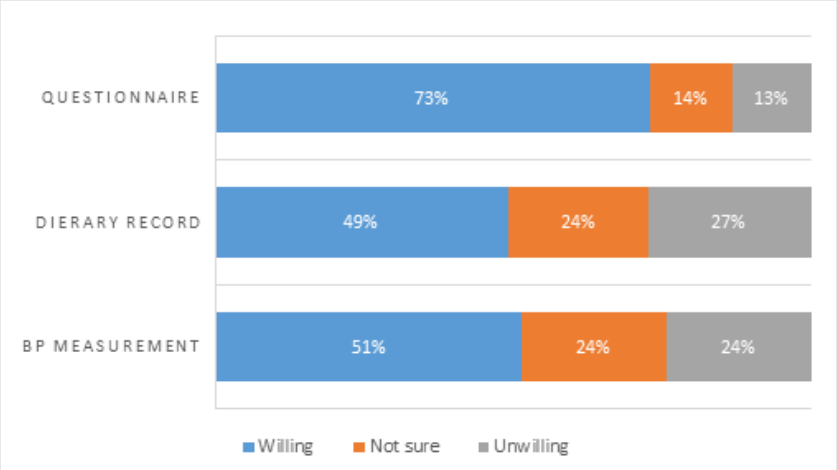
For each of the questions '*Would you be interested and click on the ad? Would you like to take part in the survey? Would you like to tell your friends about the survey?*' more than half of the participants said 'No'. 19% of the sample would be interested and click on the advert, 31% of them would like to take part in the survey, and 8% of them said they would like to tell their friends about the survey. 29 (14%) of the total sample said 'Yes' to both questions 'Would you be interested and click on the ad?' and 'Would you like to take part in the survey' (Figure 5.3).

Figure 5.3 Adolescents' attitudes on an online health survey



How willingly the participants would like to complete each part of the online health survey is shown in Figure 5.4. 68% of the participants would like to complete an online questionnaire for no more than 20 minutes, asking about age, gender, weight and lifestyle. 54% of the participants would like to complete a diet record for 3 days (10 minutes each day). 58% of the participants would like to receive a blood pressure monitor tool pack by post, learn to measure your blood pressure, record your result and then post the monitor back. However, if the participants who would like to click on the advert on Facebook and would like to take part in the online survey are taken into consideration, the percentile for those would like to complete the questionnaire, dietary survey and blood pressure measurements increased to 97%, 76% and 72% respectively.

Figure 5.4 How willingly the participants would like to complete each part of the online health survey



Ranks of factors that would make the participants more likely to complete the survey are displayed in Figure 5.5. The rank was from 1 (most influence) to 4 (least influence). '*Have your diet evaluated and receive suggestions about a healthy diet*' was ranked in first place by most of the participants, followed by 'receive a gift'. While 'Learn how to measure your blood pressure' was ranked in forth place by most of the participants. Other factors mentioned by the participants are listed in Table 5.3.

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Figure 5.5 Ranks of factors would make the participants more likely to complete the survey

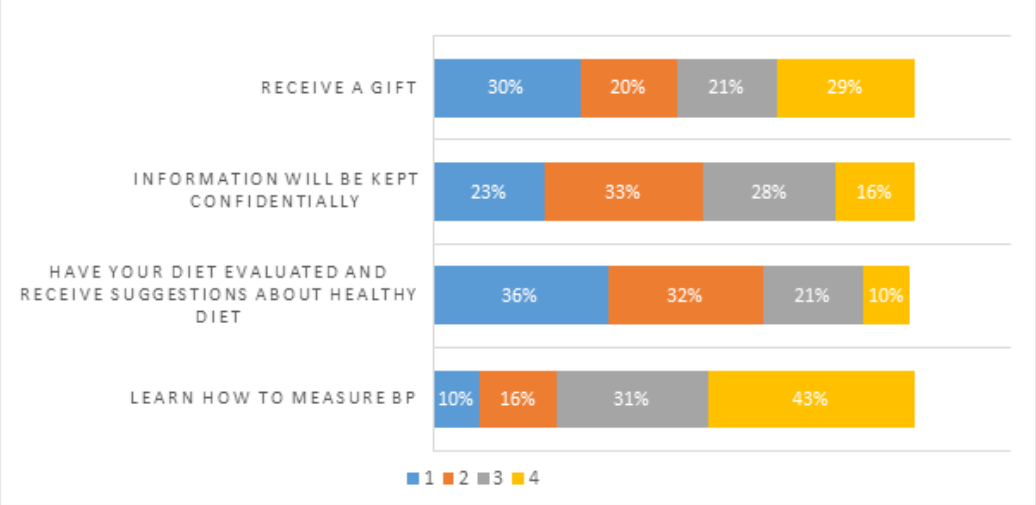

Table 5.3 Other factors will make the participants more willingly to complete the survey

Factors	N
Receive benefits	10
Receive health information	7
The survey looks trustworthy/professional	6
Know more about the survey	4
Not too long	5
My friend doing it	5
No ad pop up, no spam email following	2
Not complicated	2
Target my age group	1

Ranks of factors that would make the participants less likely to complete the survey is displayed in Figure 5.6. The rank was from 1 (most influence) to 4 (least influence). 'You will need to spend too *much time on it*' was ranked in the first place by most of the participants. '*Your parents might not allow you to do it*' was ranked the forth place by

most of the participants. Other factors mentioned by the participants are listed in Table 5.4.

Figure 5.6 Ranks of factors would make the participants less likely to complete the survey

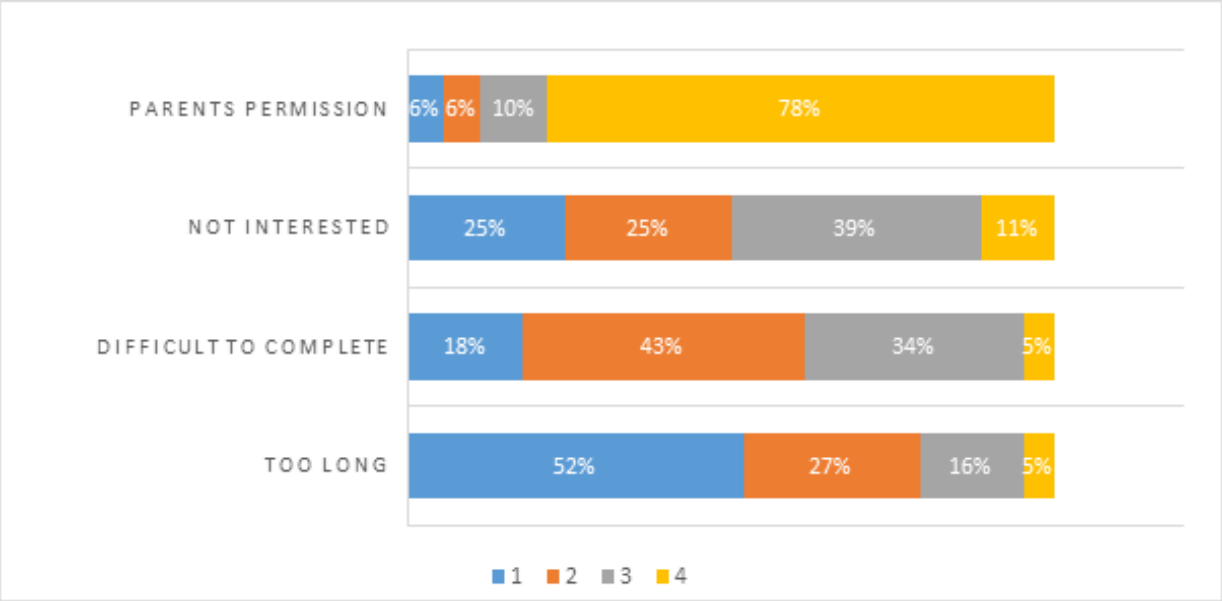

Table 5.4 Other factors will make the participants less willingly to complete the survey

Factors	N
The survey is too long	13
It does not look trustworthy	8
I will be asked about my personal information	7
Just not interested	4
I will receive spam emails or poping up ads	3
I have to pay	1
There will be invasive procedure	1
Depends on how it looks	1
Nothing returns from the survey	1

5.4.2 Part B: Web-based study

Response rate

At the end of the advert promotion, 579 participants (and their parents if necessary) signed online consent forms. 93 of them were selected randomly to complete the following parts of the study, and 55 (59.1%) of the 93 participants responded. Within the 55 participants, 2 were excluded for not reporting a valid postal address, two were excluded for being under 16 years but failing to provide parents' consent, and 1 withdrew for not having valid equipment to measure her weight and height. Fifty participants took part in the study, making the actual response rate 53.8%. Using this valid response rate, it is estimated that 311 (579*53.8%) participants would have actually taken part if all were recruited into the study.

The response rate of each part of the study is shown in Table 5.5. The response rate of completed questionnaire and blood pressure measurement was lower in the web-based stage ($p<0.001$). The response rate of completed dietary record of web-based stage were higher than school-based stage, but the difference was not statistically significant ($p=0.737$). The valid response rate of web-based stage were higher than the school-based stage, but the difference was not statistically significant ($p=0.737$).

Table 5.5 Response rate in two stages and estimated NO. of participants of each part of the study

		School-based stage		Web-based stage		Estimated NO. of participants [a]
		N	%	N	%	
Total		53		50		311
Valid participant		29	54.7%	29	58.0%	180
Questionnaire		53	100%	38	76.0%	236
Dietary record	0 day	11	20.8%	18	36.0%	112
	1 day	9	17.0%	2	4.0%	12
	2 days	4	7.5%	2	4.0%	12
	3 days	29	54.7%	29	58.0%	180
BP measurement		53	100%	38	76.0%	236

[a] estimated number of participants recruited online that would complete each part of the survey based on the response rate

Time and money expenditure

The total expenditure of adverts on social networking website was 463.36 British pounds. Expenditure for each recruited participants on adverting was £1.49, and £2.57 for each valid participant. Comparison of time and money expenditure in each stage is shown in Table 5.6.Time and money expenditure of web-based stage was calculated based on 50 recruited participants and 29 valid participants. For each valid participant, time expenditure of the web-based stage is 45% of that in school-based stage, but the money expenditure is 1.67 times of that in the school-based stage.

Table 5.6 Time and money expenditure in each stage

	School-based	**Web-based [a]**
Time in total (month)	11 months	5 months
Time per recruited participant (month)	0.21	0.02
Time per valid participant (month)	0.38	0.03
Money in total (pounds)	565	5885.46
Money per recruited participant (pounds)	10.66	18.92
Money per valid participant (pounds)	19.52	32.70

[a] the data was calculated based on the estimated number of participants in Table 5.5

Geography information

In the school-based stage, all the participants were located in Leeds. In the web-based stage, the geography range of the participants covered most of the Great Britain, which is much wider and more representative of the UK (Figure 5.7).

Figure 5.7 Locations of the participants of the ORANGE Study (online stage)

Demographic information

Comparison of demographic information of participants in each stage and in the NDNS is shown in Table 5.7, the data was calculated based only on valid participants. Compared with the NDNS, in both the school-based stage and web-based stage, fewer participants under 16 years were recruited, fewer male participants were recruited, and more white participants were recruited.

Table 5.7 Demographic information of participants in each stage and NDNS dataset

	School-based stage		Web-based stage		NDNS	
	N	**%**	**N**	**%**	**N**	**%**
Age						
14	1	3.4%	0	0.0%	275	20.0%
15	0	0.0%	3	10.3%	270	19.7%
16	3	10.3%	9	31.0%	294	21.4%
17	2	6.9%	6	20.7%	280	20.4%
18	11	37.9%	5	17.2%	209	15.2%
19	12	41.4%	6	20.7%	46	3.3%
Gender						
Male	10	34.5%	3	10.3%	656	47.7%
Female	19	65.5%	25	86.2%	718	52.3%
Missing	0	0.0%	1	3.4%	0	0.0%
Ethnicity						
White	22	75.9%	28	96.6%	921	67.0%
Non-white	7	24.1%	1	3.4%	90	6.6%
Missing	0	0.0%	0	0.0%	363	26.4%
Total	29		29		1374	

Dietary intake

Compared to the NDNS adolescent population, the online sample had lower daily intakes of energy (p=0.022), total fat (p=0.012), carbohydrates (p<0.001), sugars (p<0.001) and sodium (<0.001), while having higher daily intakes of vegetable (p<0.001). (Table 5.8)

Table 5.8 Dietary information of participants from the online survey and NDNS dataset

Nutrients	Online sample	NDNS adolescents	p value
Energy (kcal)	1601.4±546.6	1753.6±497.5	0.022*
Protein (g)	61.2±28.0	64.9±20.9	0.197
Total fat (g)	58.4±23.5	65.9±22.5	0.012*
Carbohydrates (g)	206.1±70.9	236.8±69.6	<0.001*
Sugars (g)	77.5±41.0	103.2±44.5	<0.001*
Fibre (g)	12.1±6.8	11.7±4.0	0.400
Sodium (mg)	2035.8±771.3	2164.5±740.3	<0.001*
Vegetable (g)	173.2±149.2	58.9±73.1	<0.001*
Fruit (g)	160.3±128.4	61.8±73.3	0.611

*: p<0.05 in ttest

Blood pressure levels

Compared to the NDNS adolescent population, the online sample had slightly higher SBP and DBP, but no statistically significant differences were found.(Table 5.9)

Table 5.9 Dietary information of participants from the online survey and NDNS dataset (Mean±SD)

Blood pressure	Online sample	NDNS adolescents	p value
Systolic blood pressure (mmHg)	112.5±13.5	111.3±11.1	0.43
Diastolic blood pressure (mmHg)	63.7±9.8	62.8±8.9	0.069

Feedback from participants

Thirty-one of the participants who completed the whole study gave a feedback score to the study. The average score was 8.5 out of 10. Nine of the participants gave text feedback, of which 3 were positive, while 6 gave suggestions to improve the study. Two suggested reducing spelling and/or grammar mistakes in the research materials, one suggested the researcher to create a more easily accessible website to attract more

potential participants, one suggested that the materials should all be online or all paper based, one said it was hard to find the food he/she ate on myfood24 and one said the email to confirm the postal address took a long time to arrive.

5.5 Discussion

5.5.1 Summary of Results

Most of the participants accessed the Internet and used Facebook for longer than 30 minutes per day. While using Facebook, participants were interested in the topic of *Keeping fit and exercise* (45%), *What I eat & healthy eating* (35%) and *Staying healthy* (33%). For the participants who would like to click on the advert for an online health survey on Facebook and would like to take part in the online survey, the percentile for those that would like to complete the questionnaire, dietary survey and blood pressure measurements were 97%, 76% and 72% respectively. '*Have your diet evaluated and receive suggestions about a healthy diet*' and '*receive a gift*' would increase the participants' interests in taking part in the online survey, while '*You will need to spend too much time on it*' would decrease their interests.

Compared to the school-based stage, online participants had a higher response rate in the diet record (58% vs 55%), but lower response rates in questionnaires (76% vs 100%) and blood pressure measurements (76% vs 100%). The expenditure of adverts on social networking website was £3 for each valid participant. Total money expenditure for each valid participant was £33 in the online survey, and £20 in the school-based survey. Money expenditure for each valid participants was 0.03 month in the online survey, and 0.38 month in the school-based survey.

Compared to the school-based stage, the participants of the online survey were located in a wider geography range. Compared to the standard population (NDNS adolescent population), in both the school-based survey and the web-based survey, fewer participants under 16 years were recruited, fewer male participants were recruited, and more white participants were recruited. There were significant differences between the online sample and the NDNS adolescent population in dietary intakes of energy, total fat, carbohydrates, sugars, sodium and vegetables. No differences were found in either SBP and DBP.

5.5.2 Adolescents' Internet habits and attitudes to the online survey

In the studied population, almost all of the adolescents have daily access to the Internet, and more than half of them use Facebook for longer than 30 minutes per day. Nearly half of the participants were interested in topics related with staying healthy and keeping fit, while only 6% of them were interested in the topic of heart health. These results suggest that recruiting participants for a research project exploring diet and blood pressure is possible through Facebook, but the adverts should emphasise the topics of staying healthy, keeping fit or healthy eating, rather than indicating the study is only on blood pressure.

Regarding the participants' willingness to attend the survey, 'Have your diet evaluated and receive suggestions about healthy diet' and 'receive a gift' were the two most positive affective factors, while 'You will need to spend too much time on it' was the most negative factor. This information was used in the design of web-based stage to attract more participants.

5.5.3 Comparison of online survey and traditional survey

It took 11 months to recruit enough participants in the school-based stage. The most time-consuming step was recruitment in local schools. Sending emails to schools is quick, but with low response rate. Making phone calls to schools and talking to the head-teachers who are responsible for giving consent could receive more feedback, but it is only possible at certain time of the day (lunch time and after school). After obtaining consent from the school, the study went on more effectively. In the web-based stage, the time spent on recruitment is two weeks, which is much more effective than contacting schools. In this pilot study, only one researcher carried out all the work of sending emails, preparing and posting tools, maintaining website and Facebook accounts. Time expenditure could be less if a larger study would carry out where more researchers could work simultaneously. Few studies reported the overall time spent to complete the survey, but some of them reported the average time spent on recruitment time was 0.2 month (Schwinn et al., 2017, Miller and Sønderlund, 2010), which is shorter than the time spent in the school-based stage but longer than that in the web-based stage in the ORANGE study. Although it's not possible to compare the time-efficiency of the web-based stage of ORANGE to previous studies for the variance of characteristics of the studied population and the design of the studies, it is apparent that the time-efficiency is greater than the school-based stage.

In the web-based stage, more money was spent on each valid participant. Except for advert fees and postage, the lost tools were a huge issue. In this pilot study, 60% of the blood pressure monitors were posted back to the researcher, while 40% of them were not posted back, meaning nearly £420 was lost. However, participants all around the UK were recruited through the Internet, while the school-based stage was only carried out in schools located in Leeds. However, the sample from a wider area would be more representative. If the school-based stage was expanded to throughout the UK, considerable time and transportation fees would be added to the total expenditure. In this situation, the web-based survey will show more advantages in saving money and time. Few studies reported the overall expenditure, but most of them reported the money spent on Facebook advertising. In the ORANGE study, the money spent on recruitment was £2.6 for each valid participant, it is lower than most of the previous studies. In previous studies, the amount ranged between £1.1 pounds to £84.8 (Thornton et al., 2016) in adults and, and between £0.34 to £15.53 in adolescents (Amon et al., 2014, Park and Calamaro, 2013). After investigating the design of the studies, involving adolescents, no gender limits, setting limits by the audients' interests when creating the adverts could be the factors that made the costs of the ORANGE study lower than previous studies.

Compared to the national data of NDNS, both school-based stage and web-based stage recruited a biased sample. Both of these stages recruited more participants over 16 years, more female participants and more white participants. The same has happened in previous studies. When comparing to the overall interested population, gender and age are two of the most frequently reported imbalanced factors (Thornton et al., 2016).
Ethics issues in the online survey

Informed consent

A basic standard of ethical research is that participants should be informed of the details of the study, have the chance to ask the researcher any question regarding their participation in the study, and then make informed choices about whether or not to consent to participate. In the ORANGE study, the information sheets were enclosed with the online questionnaire, including the brief description of the study, what the participants will be asked to do in the study, their rights, the potential risks and the contact details of the PhD researcher and the supervisors.

Consent from parents for participants under 16 years

If the potential participant is under 16 years, the information sheet will be emailed to their parents. Participants under 16 will be included in the study only after the consent of their parents and themselves were both obtained. However, the age and the parents' email address were all reported online. Although we asked the younger adolescents to ask their parents to fill in their contact information, there was still a risk of them lying about their details. Three participants were removed from the study for reporting the same email address for their own and their parents' address to avoid enrolling younger adolescents without parents' consent. One case of lying about their age was reported by a very unhappy parent. That participant was actually 15 years old but they reported themselves as over 16. We removed them from the study after being aware of their true age and reported the incident to the ethics committee.

In a future online survey, we suggest that Skype or phone calls can be used to make sure the parents signed the consent form. A photo or scanned copy of identity license such as passport could be provided by the participants to prove their age. Although these additional actions will increase the work of the participants and the researchers, and may have the risk of reducing the response rate, it is necessary to protect children and to ensure that young participants do not take part without consent from their guardians.

5.6 Conclusion

In a pilot online study exploring diet and blood pressure in adolescents, less time and more money was spent on each valid participant compared to a traditional school-based survey. Compared to national representative data, the online recruited sample had a higher age, more female participants and more white participants. There were significant differences between the online sample and the NDNS adolescent population in dietary intake of energy, total fat, carbohydrates, sugars, sodium and vegetables. No difference was found in blood pressure values. A protocol for a future online survey can be generated based on these useful findings.

Chapter 6. Discussion and Conclusion

6.1 Summary of findings

6.1.1 The association between diet and blood pressure in adolescents

What we already knew

Hypertension is one of the leading risk factors to health (Lim et al., 2012, Campbell et al., 2015, 2002). Although the burden of hypertension is concentrated in older populations (Rahimi et al., 2015), it is now recognised that elevated blood pressure in youth is a strong predictor of hypertension in adulthood (Sun et al., 2007, Chen and Wang, 2008, Tirosh et al., 2010). Recent epidemiological studies revealed that the prevalence of hypertension among adolescents is high and is increasing (Muntner et al., 2004, Kit et al., 2015).

Diet is one of the important factors that can affect blood pressure levels in adolescents (Sugiyama et al., 2007, Yoshinaga et al., 2011, Aounallah-Skhiri et al., 2011, Post et al., 1997, Zhu et al., 2014, Smith and Franzen-Castle, 2012, Aeberli et al., 2009, Ventura et al., 2008). After carrying out a literature review, 32 papers that explored the association between diet and blood pressure were found. Most of the studies were cross-sectional studies, and most of them used food frequency questionnaire to assess diet. Results on most of the nutrients are conflicting, and no studies on dietary vitamins were found. Future studies are required to clarify the association between diet and blood pressure in adolescents.

What we did

The National Diet and Nutrition Survey data (2008 to 2014) were used to explore cross-sectional associations between aspects of diet and blood pressure in UK adolescents. In addition, the Avon Longitudinal Study of Parents and Children (ALSPAC) was used to explore the longitudinal associations between diet and blood pressure. Vitamin E and dietary fats were selected as exposures based on the results of cross-sectional analysis.

In the regression models in both cross-sectional and longitudinal studies, systolic and diastolic blood pressure values, systolic and diastolic blood pressure Z-scores, the prevalence of hypertension were selected as outcome factors. Survival analysis was carried out in the longitudinal analysis. Confounders were included in each of the regression models.

What we added to the literature

In the NDNS adolescent population and the ALSPAC population, the prevalence of hypertension was 7%~10%.

In NDNS, after doing a general analysis by using every nutrients as exposure, using blood pressure values, blood pressure Z-scores and risk of hypertension as outcome, several dietary factors that may have relationships with adolescents' blood pressure values were identified, such as dietary vitamin E and dietary fats.

Vitamin E

In regression models, higher dietary vitamin E intake was found to have cross-sectional associations with lower systolic blood pressure, lower systolic blood pressure Z-scores and lower risk of hypertension. But higher dietary vitamin E intake was found to have longitudinal associations with increased later DBP, DBPZ, SBPZ and risk of hypertension.

Fats

In the NDNS (cross-sectional study), higher dietary trans fatty acids were linked with higher SBP and higher SBPZ. Higher dietary polyunsaturated low fat spread intake was linked with higher SBP. Higher serum total cholesterol was associated with higher SBP and SBPZ.

In ALSPAC (longitudinal study), higher dietary total fat intake was found to have longitudinal associations with increased later SBP, SBPZ and risk of hypertension. Except when blood pressure level at age 15 is considered as an outcome, higher vitamin E and total fat intakes were found to be linked with lower SBP and/or lower risk of hypertension at that age. The results on vitamin E were conflicted with the cross-sectional analysis, while the results on fats agreed with the cross-sectional analysis.

6.1.2 Online study to explore diet and blood pressure in adolescents

What we already knew

In recent decades, the proportion of adolescents who use the Internet has been increasing rapidly (Gross, 2004, Fenner et al., 2012, Gu et al., 2016, Madden et al., 2013). Social networking websites are particularly popular among adolescents(Gu et al., 2016, Madden et al., 2013, 2015b, Firth, 2017), and advertising on the Internet targeting

children and adolescents has becoming more and more popular (Strasburger and Donnerstein, 1999, Communications et al., 2006).

Carrying out medical research online is also becoming popular (Fenner et al., 2012, Gunasekaran et al., 2013, Miyagi et al., 2014, Thornton et al., 2016, Chu and Snider, 2013, Cowie and Gurney, 2018, Whitaker et al., 2017, Adam et al., 2016). Using Internet technology such as recruiting participants through Internet, online questionnaire services and online diet record (Carter et al., 2016, Cade, 2017, Carter et al., 2015, Albar et al., 2016) make medical research easier and faster(Batterham, 2014, Christofides et al., 2009, Raacke and Bonds-Raacke, 2008, Ramo and Prochaska, 2012, Fenner et al., 2012, Frandsen et al., 2016, Cantrell and Lupinacci, 2007). However, few studies was found to explore dietary factors using Internet technology.

What we did

The ORANGE (Online Research and Good Eating) study was carried out to explore the feasibility of doing online health research to study diet and blood pressure in adolescents.

Study design

The ORANGE study was composed of two stages: the school-based stage and the web-based stage (see Table 6.1). In the school-based stage, 209 participants completed the questionnaire asking about their internet habits and attitudes of online surveys. A sub-sample was selected to test the accuracy of self-measured blood pressure, and asked to complete all the other tasks (online questionnaire, online dietary survey) that will appear in the web-based stage, as a parallel sample to the web-based sample. In the web-based stage, 579 participants were recruited, and a sub-sample of 50 participants was randomly selected to complete the whole study (including online questionnaire, online diet record, self-measurements of blood pressure). The response rates, time and money expenditure, geographic and demographic information of the school-based sample and the web-based sample were compared.

Table 6.1 Study design of the ORANGE study

	Test the accuracy of self-measured BP	Attitude to online surveys	Questionnaire	Dietary record	Self-measured blood pressure
School-based Stage (n=209)		X			
-Sub sample (n=53)	X	X	X	X	
Web-based Stage (n=579)					
-Sub sample (n=50)			X	X	X

Developing blood pressure measuring method for online survey

We reviewed smart phone applications that aim to measure blood pressure, and tested 5 applications in a small pilot study. We chose a low price validated automatic blood pressure monitor (Omron PL100) and designed an instruction for the participants. Fifty three participants (a sub-sample of the school-based stage) were recruited to test the accuracy of their self-measured blood pressure using the combination of Omron PL 100 and the self-designed instruction. Based on the results of these testing studies, we compared several blood pressure measuring methods, such as using an auscultatory blood pressure monitor, using ABPM, using an automatic blood pressure monitor and using smart phone applications, in these four areas:

a. highly accessible at home or easy to be posted,
b. low price,
c. easy to operate,
d. high reliability of results,

A method was then selected for use in the online survey.

Identifying adolescents' habits of using the Internet and their attitudes to an online survey

In the school-based stage, 209 adolescents completed the questionnaire and reported their habits of using Internet and their attitudes to an online survey. The findings were used to design the web-based study.

A pilot online research studied diet and blood pressure in UK adolescents

A pilot online survey was designed based on the second part, and was carried out. The participants were recruited online through Facebook and Instagram adverts, signed consent form online (parent also signed a consent form if the participant was under 16 years), received blood pressure measuring tools by post, completed blood pressure measurements, completed questionnaires and dietary records online, then were asked to post the tools back.

What we added to the literature

Developing a blood pressure measuring method for online surveys

Compared to the readings from the standard blood pressure monitor, none of the smart phone applications can provide accurate blood pressure values. By using the selected blood pressure monitor (Omron PL100) and using the self-designed introduction, the adolescents' self-measurement of blood pressure showed acceptable agreement with standard blood pressure measurements. This method was chosen to be used in the online survey.

Identifying adolescents' habits of using the Internet and their attitudes to an online survey

Almost all of them had access to a computer or smart phone, had a Facebook account, and more than half of them spent more than 30 minutes on using Facebook. Around one third of the participants reported they would like to take part in the online survey if they saw an advert of it when using Facebook. 70% of them reported they will complete the questionnaire, half of them reported they will complete blood pressure measurement and dietary records. '*Have your diet evaluated and receive suggestions about a healthy diet*' and '*receive a gift*' would increase the participants' interests in taking part in the online survey, while '*You will need to spend too much time on it*' would decrease their interests.

A pilot online research studied diet and blood pressure in UK adolescents

Overall, 579 participants were recruited in the pilot study. Compared to the school-based stage, online participants had a higher response rate in the diet record (58% vs 55%), but lower response rates in questionnaires (76% vs 100%) and blood pressure measurements (76% vs 100%). The expenditure of adverts on social networking

website was £3 for each valid participant. Total money expenditure for each valid participant was £33 in online survey, and £20 in the school-based survey. Money expenditure for each valid participants was 0.03 month in the online survey, and 0.38 month in the school-based survey. Compared to the school-based stage, the participants of the online survey were located in a wider geographical range. Compared to the standard population (NDNS adolescent population), in both the school-based survey and the web-based survey, fewer participants under 16 years were recruited, fewer male participants were recruited and more white participants were recruited. There were significant differences between the online sample and the NDNS adolescent population in diet, the online sample took lower dietary intake of energy, total fat, carbohydrates, sugars and sodium but higher vegetables. No difference was found in either SBP or DBP.

In summary, the web-based study cost more money but less time, and the sample recruited is no worse than that in school-based sample.

6.2 Strengths and limitations

Although each chapter of this thesis has separately discussed its strengths and limitations, this section will summary the strengths and limitations of the whole project.

6.2.1 Strengths

The study is the first to use national data (NDNS) to analyse the association between diet and blood pressure in UK adolescents, and is also the first to use ALSPAC data to explore longitudinal association between diet and blood pressure in adolescents. Both of these studies generated high quality datasets, and recruited large samples. The findings from this thesis will add evidence to this area.

Few studies had reviewed the smart phone applications aiming to measure blood pressure. Although in the current study, five applications were tested only in a small pilot study, it still added new information in this area by finding none of them are suitable for scientific research and/or clinical use. The validation of adolescents' self-measured blood pressure provided evidence on self-measurements of blood pressure in UK adolescents. Using the tested blood pressure monitor (Omron PL100) and the self-designed instructions, adolescents could easily measure their own blood pressure values and be aware of their blood pressure status, which could benefit not only health research, but also household blood pressure monitoring in adolescents at risk. The

sample was a mix of local secondary school students, visiting students of the University open days and first year students at the University of Leeds. Roundhay school has students from mixed socio-economic backgrounds. Students recruited in the university also have variance backgrounds. This increased the representativeness of the study.

The ORANGE study is a novel study that explores the feasibility of using Internet technologies. The study not only tested the response rate, time and money expenditure and the representativeness of the sample, but also provides a practical protocol that can be used in future studies. The protocol of the online survey was designed based on the results from the school-based stage, where adolescents reported their Internet habits and attitudes to an online survey. It increased the consistency and effectiveness of the study.

6.2.2 Limitations

In the NDNS analysis, it is not possible to find causal relationships as it is a cross-sectional survey. In the ALSPAC analysis. The sample generated in the ALSPAC is under-representative of a non-white population, this may affect the generalization of the result (Boyd et al., 2013), and the response rate decreases at every clinic visit. However, it is still a sample large enough to run the analysis. The dietary data was derived only at age 10 and 13 years, and some confounders were only measured at baseline. It is not possible to confirm whether these factors of the participants' remained the same during the studied time. The potential changes of diet and confounders could introduce bias to the existing results. In both of the studies, dietary data was derived over a relatively short period of 3 or 4 days which may be insufficient to measure micronutrients such as variation in dietary vitamin E. Some of the samples were excluded because of missing values, which may bias the sample.

In the validation of self-measured blood pressure, although a significant sample size was reached, there are fewer younger participants under 15 years. Therefore, it may be risky when let younger adolescents measure their own blood pressure. Due to time constraints, the study was not expanded in this PhD programme. Validation in younger adolescents should be added to the current results to complete the picture.

The ORANGE study tested the feasibility of an adolescent's online survey. After analysing the results, a formal online study seems promising. The online recruited sample could be biased compared to the national data of NDNS. The online survey recruited more participants over 16 years, more female participants and more white

participants. It seemed a general issue that happened in previous studies as well. When comparing to the overall interested population, gender and age are two of the most frequently reported imbalanced factors (Thornton et al., 2016). On the other hand, a biased sample was recruited in the school-based study as well. To increase the representativeness of the online-recruited sample in future research, the adverts can be targeted to certain age/gender groups.

6.3 Perspectives and suggestions to future online surveys that explore diet and blood pressure in adolescents

According to the previous results, it is possible to generate an online survey exploring the association between diet and blood pressure. The method will allow researchers to save time and collect participants remotely across the country. Several suggestions should be taken into consideration when generating the protocol:

6.3.1 Key exposure factors

According to the cross-sectional and longitudinal analysis, dietary vitamin E intake and fats intake can be considered as key exposure factors. According to the literature review, GI/GL, calcium, fruit and vegetable intake, nuts intake, dairy intake can also be considered as exposure factors.

6.3.2 Ethical issues

There might be a risk of faking parent's consent when the participants are under 16 years. If it is necessary to recruit adolescents younger than 16, action should be taken to make sure their parents give consent. Confirming their identity by making phone calls, through facetime or skype can be used. Checking participants' identity is necessary to make sure they are over 16 years. Although these actions may reduce the response rate, they are necessary to avoid enrolling younger adolescents without their parents' consent.

6.3.3 Study design

More longitudinal studies are needed to clarify the longitudinal association between diet and blood pressure levels in adolescents. As adolescents are more likely to move to other cities to enter universities or colleges, it is of great advantage for them to be followed up online. The participants can access the online questionnaire and online diet record anywhere, and can receive blood pressure monitors by post in most areas in the

UK. They do not need to come back to the original institution to attend an appoinement. It is supposed that the response rate of follow-ups is higher in online surveys compared with traditional face-to-face survey.

6.3.4 Assessment of diet

Studies where diet records are used to measure diet can provide more dietary information, compared to those using Food Frequency Questionnaires or other questionnaires. Myfood24 is a validated tool to use to assess diet in an online survey. It is a website based tool designed to collect diet data online. Nutrition information of common foods in the UK is included in its database. Participants can access the website and record their diet easily. This online diet record tool had been validated in UK adolescents (11 - 18 years) and adults (19 – 64 years) (Carter et al., 2015). Besides, several free smart phone applications can be used to assess diet, for example my meal mate, MyFitnessPal, FatSecret, YAZIO and so on. It is important that in one study, the participants should use the same tool to assess diet to reduce system bias.

6.3.5 Advertising and recruitment

According to the results of the ORANGE study part A, these factors should be emphasized on the advert to attract more participants: a) the participants can have their diet evaluated, b) the participants will receive free gifts, c) the study is not too long. Posting adverts on weekends and on holidays will increase the response rate.

When the participants have been recruited, an email should be sent to them as soon as possible to increase the response rate.

6.4 Conclusion

The thesis studied the association between diet and blood pressure in adolescents by reviewing existing literature and analysing existing corss-sectional and longitudinal data. And tested the feasibility of carrying out an online survey to explore diet and blood pressure in UK adolescents.

In the literature review, 32 papers that explore the association between diet and blood pressure were found. Most of the studies are cross-sectional studies, and most of them used food frequency questionnaire to assess diet. Results on most of the nutrients are conflicting, no studies on dietary vitamins were found.

In the NDNS adolescent population and the ALSPAC population, the prevalence of hypertension was 7%~10%.

In the cross-sectional analysis and the longitudinal analysis, the results on vitamin E were conflicting, while the results on fats agreed with each other. In the cross-sectional study, higher dietary vitamin E intake was found to have associations with lower blood pressure levels. But in the longitudinal study, higher dietary vitamin E intake was found to have associations with increased blood pressure levels in the future. In the cross-sectional study, higher dietary trans fatty acids was linked with higher SBP levels. Higher dietary polyunsaturated low fat spread intake was linked with higher SBP levels. Higher serum total cholesterol was associated with higher SBP levels. In the longitudinal study, higher dietary total fat intake at was found to have longitudinal associations with increased blood pressure levels in the future. Except when blood pressure level at age 15 years is considered as an outcome, higher vitamin E and total fat intakes were found to be linked with lower SBP and/or lower risk of hypertension at that age.

Compared to the readings from standard blood pressure monitor, none of the smart phone applications can provide accurate blood pressure values. By using the selected blood pressure monitor (Omron PL100) and using the self-designed introduction, the adolescents' self-measurement of blood pressure shown acceptable agreement with standard blood pressure measurement. This method can be used in the online survey.

The majority of the participants in the school-based stage of the ORANGE study accessed to a computer or smart phone every day, had a Facebook account, and more than half of them spent more than 30 minutes on using Facebook. Higher percentage of the participants would be attracted to attend an online survey by Facebook adverts. '*Have your diet evaluated and receive suggestions about a healthy diet*' and '*receive a gift*' would increase the participants' interests in taking part in the online survey, while '*You will need to spend too much time on it*' would decrease their interests.

Compared to the school-based stage, online participants had a higher response rate, and were located in a wider geography range. For each valid participant, time expenditure of web-based stage is 45% of that in school-based stage, but the money expenditure is 1.67 times of that in school-based stage. Compared to the standard population (NDNS adolescent population), in both school-based survey and web-based survey, fewer

participants under 16 years were recruited, fewer male participants were recruited, and more white participants were recruited. In summary, the web-based study expensed more money but less time, and the sample recruited is no worse than that in school-based sample.

In conclusion, based on the results from this thesis, carrying out an online survey to study the association between diet and blood pressure in UK adolescents is not only meaningful but also practical.

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Table A1.1 Relationship between daily dietary saturated fatty acids intake at age 13 and later blood pressure levels

Age	Change in BP per unit change in dietary SFA intake							
	Non-adjusted models				Fully-adjusted models †			
	Coefficient	95%CI		P value	Coefficient	95%CI		P value
With systolic blood pressure								
15y	0.047	0.020	0.074	0.001*	-0.044	-0.143	0.056	0.387
17y	0.118	0.092	0.144	<0.001*	-0.001	-0.074	0.072	0.974
With diastolic blood pressure								
15y	0.027	0.005	0.048	0.016*	-0.012	-0.097	0.072	0.777
17y	-0.045	-0.062	-0.028	<0.001*	-0.050	-0.106	0.007	0.086
With systolic blood pressure Z-scores								
15y	0.002	0.000	0.005	0.074	-0.006	-0.015	0.004	0.235
17y	0.011	0.008	0.013	0.000*	-0.002	-0.009	0.005	0.666
With diastolic blood pressure Z-scores								
15y	0.001	-0.001	0.003	0.348	-0.002	-0.010	0.006	0.607
17y	-0.004	-0.006	-0.003	0.000*	-0.005	-0.010	0.001	0.088

*p<0.05 in linear regression

† Age, sex, energy intake excluding fats, sodium intake, height, BMI category, smoking, alcohol intake, SES, ethnicity were adjusted in all final models.

Table A1.2 Daily dietary saturated fatty acids intake at age 13 and later risk of hypertension

Age	Non-adjusted models				Fully-adjusted models †			
	OR	**95%CI**		**P value**	**OR**	**95%CI**		**P value**
With hypertension								
15y	1.005	0.999	1.011	0.085	0.999	0.976	1.023	0.952
17y	1.016	1.006	1.027	0.002*	1.070	0.988	1.160	0.097
Ever had hypertension	1.007	1.000	1.014	0.055	1.003	0.979	1.028	0.821

*p<0.005 in logistic regression

† Adjusted for : gender, ethnicity, BMI, alcohol intake, smoking status, sodium intake, energy intake excluding fat, parents hypertension history and household income

Table A1.3 Relationship between daily dietary MUFA intake at age 13 and later blood pressure levels

Age	Change in BP per unit change in dietary ffnp intake							
	Non-adjusted models				Fully-adjusted models †			
	Coefficient	95%CI		P value	Coefficient	95%CI		P value
With systolic blood pressure								
15y	0.068	0.034	0.102	0.000	-0.053	-0.180	0.074	0.411
17y	0.162	0.128	0.195	0.000	-0.013	-0.107	0.080	0.781
With diastolic blood pressure								
15y	0.033	0.006	0.061	0.017	-0.006	-0.114	0.103	0.919
17y	-0.042	-0.064	-0.020	0.000	-0.018	-0.090	0.055	0.634
With systolic blood pressure Z-scores								
15y	0.004	0.001	0.007	0.022	-0.007	-0.019	0.005	0.245
17y	0.015	0.011	0.018	0.000	-0.003	-0.012	0.006	0.467
With diastolic blood pressure Z-scores								
15y	0.001	-0.001	0.004	0.395	-0.002	-0.011	0.008	0.738
17y	-0.004	-0.006	-0.002	0.000	-0.002	-0.009	0.004	0.503

*$p<0.05$ in linear regression

† Age, sex, energy intake excluding fats, sodium intake, height, BMI category, smoking, alcohol intake, SES, ethnicity were adjusted in all final models.

Table A1.4 Daily dietary MUFA intake at age 13 and later risk of hypertension

Age	Non-adjusted models				Fully-adjusted models †			
	OR	95%CI		P value	OR	95%CI		P value
With hypertension								
15y	1.010	1.003	1.018	0.008	1.009	0.979	1.039	0.560
17y	1.021	1.007	1.035	0.003	1.069	0.969	1.179	0.182
Ever had hypertension	1.013	1.004	1.022	0.005	0.999	0.968	1.030	0.930

*p<0.005 in logistic regression

† Adjusted for : gender, ethnicity, BMI, alcohol intake, smoking status, sodium intake, energy intake excluding fat, parents hypertension history and household income

Table A1.5 Relationship between daily dietary PUFA intake at age 13 and later blood pressure levels

Age	Change in BP per unit change in dietary ffnp intake							
	Non-adjusted models				Fully-adjusted models †			
	Coefficient	95%CI		P value	Coefficient	95%CI		P value
With systolic blood pressure								
15y	0.128	0.073	0.183	0.000	-0.067	-0.260	0.126	0.494
17y	0.173	0.117	0.228	0.000	0.135	-0.007	0.278	0.062
With diastolic blood pressure								
15y	0.019	-0.026	0.064	0.402	-0.039	-0.203	0.125	0.642
17y	-0.020	-0.056	0.015	0.267	0.067	-0.043	0.178	0.232
With systolic blood pressure Z-scores								
15y	0.009	0.003	0.014	0.002	-0.010	-0.028	0.009	0.304
17y	0.015	0.009	0.020	0.000	0.011	-0.003	0.025	0.117
With diastolic blood pressure Z-scores								
15y	-0.001	-0.005	0.003	0.559	-0.005	-0.020	0.010	0.493
17y	-0.003	-0.006	0.001	0.097	0.005	-0.005	0.016	0.299

*p<0.05 in linear regression

† Age, sex, energy intake excluding fats, sodium intake, height, BMI category, smoking, alcohol intake, SES, ethnicity were adjusted in all final models.

Table A1.6 Daily dietary PUFA intake at age 13 and later risk of hypertension

Age	Non-adjusted models				Fully-adjusted models †			
	OR	95%CI		P value	OR	95%CI		P value
With hypertension								
Age 15	1.004	1.001	1.006	0.009	0.998	0.990	1.005	0.504
Age 17	1.009	1.004	1.013	0.001	1.015	1.002	1.028	0.023*
Ever had hypertension	1.032	1.006	1.058	0.014	0.993	0.957	1.030	0.689

*p<0.005 in logistic regression

† Adjusted for : gender, ethnicity, BMI, alcohol intake, smoking status, sodium intake, energy intake excluding fat, parents hypertension history and household income

Table A1.7 Relationship between daily dietary TFA intake at age 13 and later blood pressure levels

Age	Change in BP per unit change in dietary ffnp intake							
	Non-adjusted models				Fully-adjusted models †			
	Coefficient	95%CI		P value	Coefficient	95%CI		P value
With systolic blood pressure								
15y	0.335	0.093	0.577	0.007	-0.372	-1.172	0.428	0.361
17y	0.937	0.699	1.174	0.000	-0.187	-0.778	0.404	0.534
With diastolic blood pressure								
15y	0.206	0.011	0.402	0.039	0.147	-0.534	0.829	0.671
17y	-0.286	-0.440	-0.133	0.000	0.019	-0.440	0.479	0.934
With systolic blood pressure Z-scores								
15y	0.011	-0.012	0.035	0.330	-0.045	-0.122	0.031	0.244
17y	0.083	0.060	0.107	0.000	-0.024	-0.081	0.032	0.399
With diastolic blood pressure Z-scores								
15y	0.007	-0.010	0.025	0.406	0.006	-0.055	0.067	0.842
17y	-0.024	-0.039	-0.010	0.001	0.001	-0.041	0.044	0.956

*p<0.05 in linear regression

† Age, sex, energy intake excluding fats, sodium intake, height, BMI category, smoking, alcohol intake, SES, ethnicity were adjusted in all final models.

Table A1.8 Daily dietary TFA intake at age 13 and later risk of hypertension

Age	Non-adjusted models				Fully-adjusted models †			
	OR	95%CI		P value	OR	95%CI		P value
With hypertension								
15y	1.032	0.978	1.090	0.245	1.052	0.858	1.289	0.625
17y	1.126	1.025	1.236	0.014	1.018	0.564	1.838	0.952
Ever had hypertension	1.038	0.975	1.105	0.248	0.971	0.790	1.193	0.777

*p<0.005 in logistic regression

† Adjusted for : gender, ethnicity, BMI, alcohol intake, smoking status, sodium intake, energy intake excluding fat, parents hypertension history and household income

Table A1.9 Relationship between daily dietary PUFA cooking oil and margarine intake at age 13 and later blood pressure levels

Age	Change in BP per unit change in dietary ffnp intake							
	Non-adjusted models				Fully-adjusted models †			
	Coefficient	95%CI		P value	Coefficient	95%CI		P value
With systolic blood pressure								
15y	0.039	0.002	0.076	0.038	-0.040	-0.155	0.076	0.500
17y	0.055	0.018	0.092	0.004	0.157	0.071	0.243	0.000
With diastolic blood pressure								
15y	0.015	-0.015	0.045	0.320	0.012	-0.086	0.109	0.813
17y	0.026	0.002	0.050	0.033	0.107	0.042	0.173	0.001
With systolic blood pressure Z-scores								
15y	0.002	-0.001	0.006	0.201	-0.003	-0.014	0.008	0.611
17y	0.003	0.000	0.007	0.065	0.017	0.009	0.025	0.000
With diastolic blood pressure Z-scores								
15y	0.001	-0.002	0.004	0.482	0.002	-0.007	0.010	0.730
17y	0.002	-0.001	0.004	0.179	0.010	0.004	0.016	0.002

*p<0.05 in linear regression

† Age, sex, energy intake excluding fats, sodium intake, height, BMI category, smoking, alcohol intake, SES, ethnicity were adjusted in all final models.

Table A1.10 Daily dietary PUFA cooking oil and margarine intake at age 13 and later risk of hypertension

Age	Non-adjusted models				Fully-adjusted models †			
	OR	95%CI		P value	OR	95%CI		P value
With hypertension								
15y	1.004	0.996	1.012	0.354	1.012	0.984	1.042	0.396
17y	1.021	1.007	1.034	0.003	1.132	1.066	1.202	0.000
Ever had hypertension	1.006	0.997	1.016	0.210	1.025	0.995	1.056	0.106

*p<0.005 in logistic regression

† Adjusted for : gender, ethnicity, BMI, alcohol intake, smoking status, sodium intake, energy intake excluding fat, parents hypertension history and household income

Table A1.11 Relationship between daily dietary Un-PUFA cooking oil and margarine intake at age 13 and later blood pressure levels

Age	Change in BP per unit change in dietary ffnp intake							
	Non-adjusted models				Fully-adjusted models †			
	Coefficient	95%CI		P value	Coefficient	95%CI		P value
With systolic blood pressure								
15y	-0.009	-0.052	0.034	0.673	0.113	-0.047	0.272	0.165
17y	0.021	-0.021	0.063	0.332	-0.064	-0.181	0.054	0.286
With diastolic blood pressure								
15y	0.015	-0.020	0.049	0.409	-0.019	-0.154	0.115	0.777
17y	-0.002	-0.030	0.025	0.872	0.020	-0.069	0.109	0.653
With systolic blood pressure Z-scores								
15y	-0.002	-0.006	0.002	0.293	0.009	-0.006	0.024	0.258
17y	0.002	-0.002	0.006	0.305	-0.008	-0.020	0.003	0.140
With diastolic blood pressure Z-scores								
15y	0.000	-0.003	0.004	0.764	-0.003	-0.015	0.009	0.621
17y	0.000	-0.003	0.003	0.965	0.001	-0.007	0.009	0.787

*p<0.05 in linear regression

† Age, sex, energy intake excluding fats, sodium intake, height, BMI category, smoking, alcohol intake, SES, ethnicity were adjusted in all final models.

Table A1.12 Daily dietary Un-PUFA cooking oil and margarine intake at age 13 and later risk of hypertension

Age	Non-adjusted models				Fully-adjusted models †			
	OR	95%CI		P value	OR	95%CI		P value
With hypertension								
15y	0.999	0.990	1.009	0.895	1.044	0.990	1.101	0.115
17y	1.004	0.987	1.022	0.656	1.029	0.990	1.069	0.152
Ever had hypertension	1.004	0.993	1.015	0.492	1.017	0.974	1.062	0.445

*p<0.005 in logistic regression

† Adjusted for : gender, ethnicity, BMI, alcohol intake, smoking status, sodium intake, energy intake excluding fat, parents hypertension history and household income

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MaPS and Engineering joint Faculty Research Ethics Committee (MEEC FREC)
University of Leeds

29 November 2018

Dear Ziyi Li

Title of study **The ORANGE study: Online Research of Adolescents and Good Eating (School-based stage)**
Ethics reference **MEEC 15-030**

I am pleased to inform you that the application listed above has been reviewed by the MaPS and Engineering joint Faculty Research Ethics Committee (MEEC FREC) and following receipt of your response to the Committee's previous comments, I can confirm a favourable ethical opinion as of the date of this letter. The following documentation was considered:

Document	Version	Date
MEEC 15-030 Response.doc	1	21/03/16
MEEC 15-030 Ethical_Review_Form_V2.docx	2	21/03/16
MEEC 15-030 Appendix_1_Recruiting_Email_to_School_V2.doc	2	21/03/16
MEEC 15-030 Appendix_2_Poste_V2.pptx	2	21/03/16
MEEC 15-030 Appendix_3_Information_Sheet_for_School-based_Survey_V2.docx	3	06/04/16
MEEC 15-030 Appendix_4_Consent_Form_for School-based_Survey_V2.doc	3	06/04/16
MEEC 15-030 Appendix_5_Questionnaire_V2.doc	3	06/04/16
MEEC 15-030 Appendix_6_ Blood_Pressure_Mearsurement_Instruction_V1.doc	2	21/03/16
MEEC 15-030 Appendix_7_Letter_to_GP_V1.doc	2	21/03/16
MEEC 15-030 Appendix_8_Risk_Assessment_Form_V1.doc	2	21/03/16
MEEC 15-030 DBS_ZiyiLi.pdf	2	21/03/16

Please notify the committee if you intend to make any amendments to the original application as submitted at date of this approval as all changes must receive ethical approval prior to implementation. The amendment form is available at http://ris.leeds.ac.uk/EthicsAmendment.

Please note: You are expected to keep a record of all your approved documentation. You will be given a two week notice period if your project is to be audited. There is a checklist listing examples of documents to be kept which is available at http://ris.leeds.ac.uk/EthicsAudits.

We welcome feedback on your experience of the ethical review process and suggestions for improvement. Please email any comments to ResearchEthics@leeds.ac.uk.

Yours sincerely

Jennifer Blaikie
Senior Research Ethics Administrator, Research & Innovation Service
On behalf of Professor Gary Williamson, Chair, MEEC FREC

CC: Student's supervisor(s)

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MaPS and Engineering joint Faculty Research Ethics Committee (MEEC FREC)
University of Leeds

29 November 2018

Dear Ziyi Li

Title of study **The ORANGE study: Online Research of Adolescents and Good Eating (School-based stage)**
Ethics reference **MEEC 15-030, amendment June 2016**

I am pleased to inform you that the amendment to the application listed above has been reviewed by the Chair of the MaPS and Engineering joint Faculty Research Ethics Committee (MEEC FREC) and I can confirm a favourable ethical opinion as of the date of this letter. The following documentation was considered:

Document	Version	Date
MEEC 15-030 amendment June 2016 Amendment_form_MEEC 15-030_06062016.pdf	1	06/06/16
MEEC 15-030 amendment June 2016 Appendix_1_Recruiting_Email_to_School_V3_06062016.doc	1	06/06/16
MEEC 15-030 amendment June 2016 Appendix_3_Information_Sheet_for_School_based_Survey_V4_06062016.docx	1	06/06/16
MEEC 15-030 Response.doc	1	21/03/16
MEEC 15-030 Ethical_Review_Form_V2.docx	2	21/03/16
MEEC 15-030 Appendix_1_Recruiting_Email_to_School_V2.doc	2	21/03/16
MEEC 15-030 Appendix_2_Poste_V2.pptx	2	21/03/16
MEEC 15-030 Appendix_3_Information_Sheet_for_School-based_Survey_V2.docx	3	06/04/16
MEEC 15-030 Appendix_4_Consent_Form_for School-based_Survey_V2.doc	3	06/04/16
MEEC 15-030 Appendix_5_Questionnaire_V2.doc	3	06/04/16
MEEC 15-030 Appendix_6_ Blood_Pressure_Mearsurement_Instruction_V1.doc	2	21/03/16
MEEC 15-030 Appendix_7_Letter_to_GP_V1.doc	2	21/03/16
MEEC 15-030 Appendix_8_Risk_Assessment_Form_V1.doc	2	21/03/16
MEEC 15-030 DBS_ZiyiLi.pdf	2	21/03/16

Please notify the committee if you intend to make any further amendments to the original research as submitted at date of this approval, including changes to recruitment methodology. All changes must receive ethical approval prior to implementation. The amendment form is available at http://ris.leeds.ac.uk/EthicsAmendment.

Please note: You are expected to keep a record of all your approved documentation, as well as documents such as sample consent forms, and other documents relating

to the study. This should be kept in your study file, which should be readily available for audit purposes. You will be given a two week notice period if your project is to be audited. There is a checklist listing examples of documents to be kept which is available at http://ris.leeds.ac.uk/EthicsAudits.

We welcome feedback on your experience of the ethical review process and suggestions for improvement. Please email any comments to ResearchEthics@leeds.ac.uk.

Yours sincerely

Jennifer Blaikie
Senior Research Ethics Administrator, Research & Innovation Service
On behalf of Professor Gary Williamson, Chair, MEEC FREC

CC: Student's supervisor(s)

UNIVERSITY OF LEEDS

Nutritional Epidemiology Group

School of Food Science

Information Sheet of The ORANGE Study

Online Research of Adolescents and Good Eating

Hello !

You are being invited to take part in the ORANGE Study: Online Research of Adolescents and Good Eating. Before you decide if you want to take part it is important for you to understand why the research is being done and what it will involve.

Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Ethical approval obtained from the Research Ethics Committee of Faculty of Mathematics and Physical Sciences (NO: MEEC 15-030)

Purpose of the research

In traditional surveys exploring diet and blood pressure, face-to-face interviews are necessary to collect data and measure blood pressure. In this research, a novel web-based study method will be developed aimed at teenagers.

In this stage of the project I aim:

- to test the accuracy of self-measured blood pressure in teenagers,
- to collect the participants' attitude to an online survey
- to collect their diet data, general information and blood pressure data.

This will help me to test the feasibility to recruit participants through social networking websites, to collect information using online questionnaire and online diet record website and obtain blood pressure data remotely in 13-19 year old UK teens.

Your rights in the study

- It is up to you to decide whether or not to take part.
- If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form.
- You can drop out of the study at any time without it affecting you in any way. You do not have to give a reason.
- All the information that we collect from you during the course of this research will be kept strictly in secret. The information including: your contact detail, name, age, gender and the questionnaire you complete. You will not be able to be identified in any reports or publications, and the data will be reported without any names.

What will happen to you if take part

- The study will be carried out in a safe, separate, warm and quiet room in your school.
- It will take 25-40 minutes, plus 10-15 minutes to record your diet the next day.

More details in the next page

Continue

What will happen to you if take part

There are 5 things you will need to do in the research

Read this Information Sheet and the Consent Form carefully and give consent before taking part. Your parents also need to give consent if you are under 16.

You'll need to complete an online questionnaire about your general information, information related with blood pressure (e.g. smoking status, alcohol intake, physical activities, etc.) and your attitude to an online survey. Your height and weight will be measured as well.

Your blood pressure will be measured. I'll give you a pack of tools and an introduction, and let you measure their blood pressure yourself.
When you finish your measurement, I'll measure your blood pressure using the same blood pressure monitor.
You will need to remove your clothes that cover your upper arm by rolling up your sleeve or removing jacket/jumper.

Your height and weight will be measured.

All the steps above will be take place in your school.

You will need to record your daily diet on myfood24 for 3 days at home.

More details in the next page

Continue

The possible disadvantage and benefits to you

There will be no risk for taking part in this research, but you might feel a little uncomfortable (arm squeezed) while your blood pressure is being measured by the blood pressure monitor with an arm band.

Taking blood pressure measurements may potentially reveal cases of high blood pressure. In this case, you and your parents will be given a letter advising you to make an appointment with your GP. At the same time, you will learn about how to measure blood pressure properly during the program.

Whilst there are no other immediate benefits for you, it is hoped that this work will improve the development of novel blood pressure measuring methods and our understanding of how this relates to lifestyle and health in adolescents.

Who is organising the research?

The research is organised by the Nutritional Epidemiology Group, the School of Food Science and Nutrition, the University of Leeds.

Contact information

PhD researcher	Ziyi Li: fszl@leeds.ac.uk Room G.07 Food Science Building University of Leeds
Supervisor	Charlotte Evans: C.E.L.Evans@leeds.ac.uk Janet Cade: J.E.Cade@leeds.ac.uk

Thank you!

You will be given a copy of this information sheet, and thanks again for reading the information sheet and considering taking part in the ORANGE study. If you would like to take part in the study, please tell your teacher or contact me (fszl@leeds.ac.uk).

Bye!

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Consent Form for Participants

The ORANGE Study: Online Research of Adolescents and Good Eating

- I confirm that I have read and understand the information explaining the above research project and I have had the opportunity to ask questions about the project.
- I agree for the data collected from me to be stored and used in relevant future research in an anonymised form.
- I understand that relevant sections of the data collected during the study, may be looked at by individuals from the University of Leeds or from regulatory authorities where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.
- I agree to take part in the above research project.

Please sign the consent form if you agree with the above statements.
Please return the consent form together with the questionnaire.

Your name	
Your signature	
Date	
Name of lead researcher	Ziyi Li
Signature	
Date	

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Consent Form for Parents/Guardians

The ORANGE Study: Online Research of Adolescents and Good Eating

- I confirm that I have read and understand the information explaining the above research project and I have had the opportunity to ask questions about the project.
- I agree for the data collected from me and my child to be stored and used in relevant future research in an anonymised form.
- I understand that relevant sections of the data collected during the study, may be looked at by individuals from the University of Leeds or from regulatory authorities where it is relevant to my child's and my taking part in this research. I give permission for these individuals to have access to my child's and my records.
- I give consent for my child and me to take part in the above research project and will inform the lead researcher (Ziyi Li) should my contact details change.

Sign if you agree with the statements above.

Name of parent/guardians	
Relationship with the child	
Parent/guardian's signature	
Date	
Name of lead researcher	Ziyi Li
Signature	
Date	

School of Food Science and Nutrition
UNIVERSITY OF LEEDS

Consent Form for Schools

The ORANGE Study: Online Research of Adolescents and Good Eating (school-based stage)

	Add your initials next to the statements if you agree
I confirm that I have read and understand the information explaining the above research project and I have had the opportunity to ask questions about the project.	
I agree for the data collected from the students to be stored and used in relevant future research in an anonymised form. I agree to keep the data confidentially.	
I agree to help in communication with students and provide proper venue for the study.	
I give consent for the researchers to carry out this study in the school.	

Name of school	
Name of teacher	
Teacher's signature	
Date	
Name of lead researcher	
Signature	
Date	

Appendix 7: Poster (ORANGE study: school-based stage)

Take part in the ORANGE study

Online Research of Adolescents and Good Eating

Hello! You are invited to take part in **the ORANGE study,** if your age is **19 or under.**

What do you need to do

1. Complete a questionnaire
2. Receive an instruction and measure your own blood pressure
3. Have your height, weight and blood pressure measured by the researcher (task 1-3 will take 25 minutes)
4. Record your diet online for 3 days (10 minutes/day)

What will you gain

1. £5 voucher
2. Have your diet analysed

How to take part

Email us !

Ziyi Li
PhD student
fszl@leeds.ac.uk
School of Food Science and Nutrition
UNIVERSITY OF LEEDS

Ethical approval Obtained from the Research Ethics Committee of Faculty of Mathematics and Physical Sciences NO: MEEC 15-030

Appendix 8: Script for phone recruitment for the schools

Hello, it's University of Leeds. It's a follow up of an email last week about your school participating in a health research study. May I speak to the person in charge of science please?

no

May I have the email address of the science teacher please?

When should I call again?

(if they'll call back) Yes, please call Leslie 07759351896

yes

Hello, it's University of Leeds. I'm calling to ask would you like to take part in a health research study?

(key points:)

I wish to recruit 30 students in your school, and your school will receive 100 pounds voucher as thanks for your time and help.

In the study, each recruited student will attend a 50 minutes interview, including a questionnaire, and measurement of height, weight and blood pressure. There will be no risk for your students, and all the information will be kept strictly confidentially.

What you need to do is to provide a space with at least 3 computers, and help me to get in touch with students.

May I attend one of the science class and talk about my study for 5 to 10 minutes?

Before hanging up

May I have your email address please?

Shall we have a brief meeting this week or next week? What time is good for you?

When should I call again?

Yes, please call Leslie 07759351896.

Make notes

Instruction: how to measure blood pressure?

With this easy to follow introduction, you are sure to measure your blood pressure correctly. Just read and follow each step carefully.

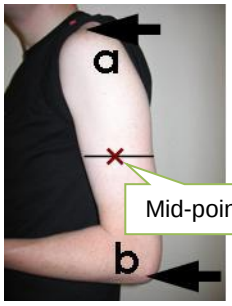
1. Sit still at a table or desk to rest yourself for 10-15 minutes (you may do this while completing the questionnaire or reading these instructions).

2. Check you have the measuring tools beside you.

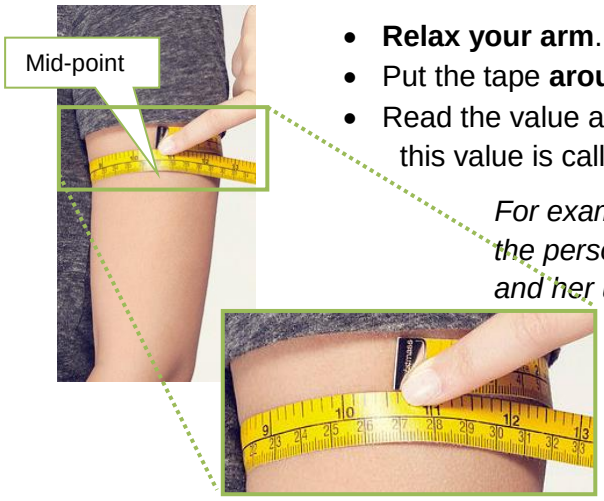
3. Choose the arm & correct size of blood pressure arm band

Choose the arm which you **do NOT use to write.** Please tick the right answers.

Which hand you use to write	☐Left ☐Right
Which upper arm you have chosen now	☐Left ☐Right



- Remove your clothes covering your upper arm
- Put the tape measure from **point 'a' (on your shoulder)** to **point 'b' (on your elbow),** measure the length of your upper arm and write it down here _____cm
- Find the **mid-point** of your upper arm and mark it with the water-erasable pen



- **Relax your arm**.
- Put the tape **around** your arm at the **mid-point**
- Read the value and write it down here : _____cm, this value is called your <u>upper arm circumference</u>.

For example,
the person in the picture should write 27,
and her upper arm circumference is 27cm.

- Read the table below and **decide which cuff suits you** according to your <u>upper arm circumference</u> you just measured.
- If you need a small or large cuff, stop measuring your blood pressure, go to the online questionnaire, click Next, answer the questions and then request a cuff that suits you.

Arm band size	**<u>Upper Arm Circumference</u>**
Small	22cm and under
Normal	23cm – 34cm
Large	Over 34cm

Turn to the next page

Appendix 9: Instruction for blood pressure self-measurement

4. Attach the arm band to the blood pressure monitor

Find the end of the tube.

Find the hole on the left side of the monitor.

Insert the end into the hole.

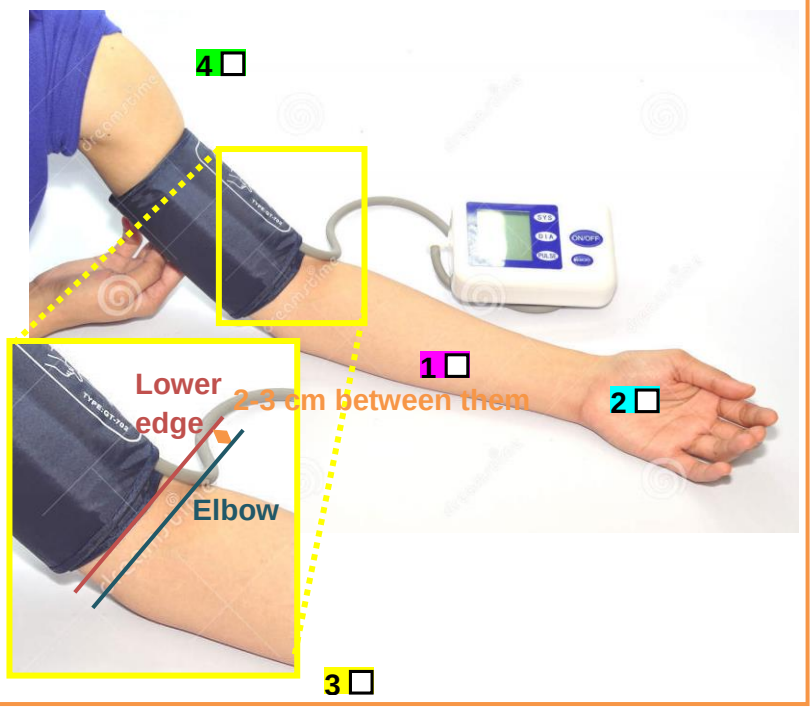
5. Wear the arm band. Please **check** the 4 points making sure you have done the right thing.

1. Your arm is **put on a table or desk** and **relaxed**.

2. Your palm is facing **upward**.

3. Put your arm through the arm band. Pull the arm band up so that the lower edge of the cuff is about **2-3 cm above your elbow**.

4. Tighten the arm band using the Velcro flap. Make sure you can just put 2 fingers between the arm band and your arm. Adjust the arm band if it's too tight or too loose.



6. Measure your blood pressure

Attention: you will feel a slight squeezing on your arm when the arm band is filling with air, don't be scared, this is normal. ☺ Make sure you have a pen with you. Now please put the arm wearing the arm band on the desk and relax. Try to keep sitting still and don't talk when measuring your blood pressure.

Turn on the blood pressure monitor (press O/I) with your free hand and the measurement will start automatically. You can see the values on the screen are changing. Wait for the cuff to deflate. When the numbers on the screen stop flashing (it may take a few seconds), write them down in the box on the right→	SYS: _____mmHg DIA: _____mmHg
Wait for one minute. Keep sitting still. You can use the hourglass.	
Press START (you may need to press it twice) on the blood pressure monitor and measure your blood pressure again as before. (*Don't worry if the numbers are not same as the first measurement – our blood pressure is always changing, that's why we need 3 measurements to get the average value of your blood pressure.)* Write down the numbers→	SYS: _____mmHg DIA: _____mmHg
Wait for one minute. Keep sitting still.	
Press START (you may need to press it twice) on the blood pressure monitor and measure your blood pressure for a third time. Write down the numbers →	SYS: _____mmHg DIA: _____mmHg

Well done! Now you know how to measure your blood pressure yourself!

Research & Innovation Service
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Leeds, LS2 9NL
Tel: 0113 343 4873
Email: ResearchEthics@leeds.ac.uk

UNIVERSITY OF LEEDS

Ziyi Li
School of Food Science and Nutrition
University of Leeds
Leeds, LS2 9JT

MaPS and Engineering joint Faculty Research Ethics Committee (MEEC FREC)
University of Leeds

23 February 2017

Dear Ziyi Li

Title of study **The ORANGE study: Online Research of Adolescents and Good Eating (Web-based stage)**
Ethics reference **MEEC 16-002, response 2**

I am pleased to inform you that the application listed above has been reviewed by the MaPS and Engineering joint Faculty Research Ethics Committee (MEEC FREC) and following receipt of your response to the Committee's initial comments, I can confirm a favourable ethical opinion as of the date of this letter. The following documentation was considered:

Document	Version	Date
MEEC 16-002 Committee Provisional.doc (response)	1	21/11/16
MEEC 16-002 Ethical_Review_Form_V2.doc	2	21/11/16
MEEC 16-002 Appendix_2_ Blood_Pressure_Mearsurement_Instruction_V2.doc	2	21/11/16
MEEC 16-002 Appendix_6_Questionnaire_V2.doc	2	21/11/16
MEEC 16-002 Appendix_8_How_to_get_consents_V1.docx	1	21/11/16
MEEC 16-002 Appendix_1_DBS_ZiyiLi_V1.pdf	1	01/09/16
MEEC 16-002 Appendix_3_Example_of_Advertsement_V1.pptx	1	01/09/16
MEEC 16-002 Appendix_4_Information_Sheet_V1.doc	1	01/09/16
MEEC 16-002 Appendix_5_Consent_Form_V1.doc	1	01/09/16
MEEC 16-002 Appendix_7_Letter_to_GP_V1.doc	1	01/09/16
MEEC 16-002 Appendix_8_How_to_get_consents_V2.docx	3	01/02/17
MEEC 16-002 Ethical_Review_Form_V3.doc	3	01/02/17

The Committee have made the following comments with changes that are required in relation to recruitment:

- You are obviously keen to assess the use of online recruitment as part of your methodology and this will carry the risk of participants not being who they say they are, and therefore potentially not gaining parental consent It is important to show that reasonable steps have been taken to try and control the issue regarding parental consent and using an email address is not sufficient. A confirmatory phone call to the parents or guardians would provide a more robust method of doing this than an email. is the committee would prefer this to be done by phone, but it would need to be made clear to the

parent/guardian on the consent form that in agreeing to their child taking part in the study then they are also agreeing to their mobile number (which is being collected anyway; Appendix 8, p3), being used by the researchers for confirmation of relationship/address etc.

Please notify the committee if you intend to make any amendments to the original application as submitted at date of this approval as all changes must receive ethical approval prior to implementation. The amendment form is available at http://ris.leeds.ac.uk/EthicsAmendment.

Please note: You are expected to keep a record of all your approved documentation. You will be given a two week notice period if your project is to be audited. There is a checklist listing examples of documents to be kept which is available at http://ris.leeds.ac.uk/EthicsAudits.

We welcome feedback on your experience of the ethical review process and suggestions for improvement. Please email any comments to ResearchEthics@leeds.ac.uk.

Yours sincerely

Victoria Butterworth
Research Ethics Administrator, Research & Innovation Service
On behalf of Dr Dawn Groves, Chair, MEEC FREC

CC: Student's supervisor(s)

Research & Innovation Service
Level 11, Worsley Building
University of Leeds
Leeds, LS2 9NL
Tel: 0113 343 4873
Email: ResearchEthics@leeds.ac.uk

UNIVERSITY OF LEEDS

Ziyi Li
School of Food Science and Nutrition
University of Leeds
Leeds, LS2 9JT

MEEC Faculty Research Ethics Committee
University of Leeds

16 May 2017

Dear Ziyi

Title of study **The ORANGE study: Online Research of Adolescents and Good Eating (Web-based stage)**
Ethics reference **MEEC 16-002 Amendment May 17**

I am pleased to inform you that the amendment to the application listed above has been reviewed by the Chair of the MaPS and Engineering joint Faculty Research Ethics Committee (MEEC FREC) I can confirm a favourable ethical opinion as of the date of this letter. The following documentation was considered:

Document	*Version*	*Date*
MEEC 16-002 amendment May 2017 Amendment_form_MEEC 16-002 (2)	1	03/05/2017
MEEC 16-002 amendment May 2017 Amendment_form_MEEC 16-002	1	03/05/2017
MEEC 16-002 amendment May 2017 Appendix_3_Example_of_Advertsement_for_Parents	1	03/05/2017
MEEC 16-002 amendment May 2017	1	03/05/2017

Please notify the committee if you intend to make any further amendments to the original research as submitted at date of this approval, including changes to recruitment methodology. All changes must receive ethical approval prior to implementation. The amendment form is available at http://ris.leeds.ac.uk/EthicsAmendment.

Please note: You are expected to keep a record of all your approved documentation, as well as documents such as sample consent forms, and other documents relating to the study. This should be kept in your study file, which should be readily available for audit purposes. You will be given a two week notice period if your project is to be audited. There is a checklist listing examples of documents to be kept which is available at http://ris.leeds.ac.uk/EthicsAudits.

We welcome feedback on your experience of the ethical review process and suggestions for improvement. Please email any comments to ResearchEthics@leeds.ac.uk.

Yours sincerely

Victoria Butterworth
Research Ethics Administrator, Research & Innovation Service
On behalf of Dr Dawn Groves, Chair, MEEC FREC
CC: Student's supervisor(s)

Hello! You are invited to the ORANGE study, please take time to read the following information. Please ask us if you would like more information.

Aim of the study

The aim of the study is to test the feasibility of

- recruiting participants through social networking websites,
- collecting information using online questionnaire and online diet record website
- obtaining blood pressure data remotely in 13-19 year old UK teens.

What do you need to do and your rights

In the study, you will need to

- complete an online questionnaire (it will take approximately 10-15 minutes) about your generel information (for example age, ethnity, smoking habits, alcohol intake habits, physical activities, etc.) and diet
- receive a pack of tool by post to measure your own blood pressure, and then post it back. You do not need to pay the postage
- record your diet online for 3 days (approximately 10 minutes per day).

You can withdraw the study at any time without it affecting you in any way. You do not have to give a reason.

Possible disadvantages and benefits

There will be no risk for taking part in this research, all the information that we collect from you during the course of this research will be kept strictly in secret. You will not be able to be identified in any reports or publications, and the data will be reported without any names.

You can have yor diet analysed and receive £5 Amazon Voucher as a thanks to your time and efforts.

About the research team

The research is organised by the Nutritional Epidemiology Group, the School of Food Science and Nutrition, the University of Leeds. Ethical approval has been obtained from the Research Ethics Committee of Faculty of Mathematics and Physical Sciences (ref. no. MEEC 16-002)

PhD researcher :
Ziyi Li
fszl@leeds.ac.uk
Room G.07
Food Science Building
University of Leeds

Supervisors:
Charlotte Evans: C.E.L.Evans@leeds.ac.uk
Janet Cade: J.E.Cade@leeds.ac.uk

Please read the following statements:

- I confirm that I have read and understand the information explaining the above research project and I have had the opportunity to ask questions about the project.
- I agree for the data collected from me to be stored and used in relevant future research in an anonymised form.
- I understand that relevant sections of the data collected during the study, may be looked at by individuals from the University of Leeds or from regulatory authorities where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.
- I agree to take part in the above research project.

Please note that if you are under 16 years, we cannot include you in the study unless we receive your parent's consent as well.

Please select "Yes" if you agree with the above statements. Otherwise please select "No"

Yes
No

Please read the following statements:

- I confirm that I have read and understand the information explaining the above research project and I have had the opportunity to ask questions about the project.
- I agree for the data collected from my child to be stored and used in relevant future research in an anonymised form.
- I understand that relevant sections of the data collected during the study, may be looked at by individuals from the University of Leeds or from regulatory authorities where it is relevant to my child's taking part in this research. I give permission for these individuals to have access to my child's records.
- I agree my child to take part in the above research project.

Please select "Yes" if you agree with the above statemen. Otherwise please select "No"

Yes

No

The ORANGE Study: Online Research of Adolescents and Good Eating

Teenagers' Questionnaire (A)

Date	dd/mm/yyyy		
Your email address (optional)			
Your gender		**Your age**	

Hello! Thanks for taking part in the ORANGE Study. We would like to know something about your Internet habits and your attitudes to an online survey.

1. Do you have daily access to a computer? ☐Yes ☐No

2. Do you have a smartphone? ☐Yes ☐No

3. Which of the following websites/apps do you use regularly (that means at least once a week)? Please tick all that apply.

   ☐Facebook ☐Youtube ☐Snapchat
   ☐Twitter ☐Google+ ☐Whatsapp
   ☐Tumblr ☐Instagram
   ☐Others, please specify_____

4. Do you have a Facebook account? ☐Yes ☐No

5. Did you use Facebook in the last week? ☐Yes ☐No

6. How long, in the last week, have you spent using Facebook each day?

   ☐30 minutes or less ☐1 hour or less but more than 30 minutes
   ☐2 hours or less but more than 1 hour ☐More than 2 hours

7. When using Facebook or other social media sites, which of the following topics are you interested in? Tick all that apply.

   ☐Staying healthy ☐What I eat and healthy eating
   ☐Losing weight ☐Keeping fit and exercises
   ☐Heart health (for example blood pressure) ☐None of them

Questions 8 to 13.a are about your attitudes to an online survey. Imagine that you are using Facebook (or looking at other websites), and an advert (for example the one on the right) jumps out at you. The ad is about an online diet and health survey calling for participants to take part.

8. Would you be interested and click on the ad?
   ☐Yes ☐No ☐Not sure
9. Would you like to take part in that survey?
   ☐Yes ☐No ☐Not sure
10. Would you like to tell your friends about that survey?
    ☐Yes ☐No ☐Not sure

Turn to the next page

11. Here are three parts of the survey, think about how willing you would be to complete each part. Please tick the boxes that best describes your views.

	Very Willing	Willing	Not sure	Unwilling	Very Unwilling
Complete a questionnaire about you. (It will take no more than 20 minutes, asking about your age, gender, weight, lifestyle, etc.)					
Record your diet online for 3 days (10 minutes per day)					
Receive a blood pressure monitor tool pack by post, learn to measure your blood pressure, record your result and then post the monitor back (you do not have to pay the postage)					

12. Please rank the following statements in order of which would make you most likely to complete the survey. Rank each statement from 1st (most likely) to 4th (least likely) to influence you.

Rank	Statements
	You can learn about how to measure blood pressure
	Your daily diet will be evaluated and you'll receive suggestions about healthy diet
	Your information will be kept confidentially
	You will receive a gift when completing the survey

12.a Is there anything else that would make you more likely to take part and complete the survey? Please write as many reasons as possible:

13. Please rank the following statements in order of which would make you less likely to complete the survey. Rank each from 1st (most annoying) to 4th (least annoying).

Rank	Statements
	You will need to spend too much time on it
	It looks difficult to complete
	Just not interested in it.
	Your parents might not allow you to do it.

13.a Is there anything else that would make you less likely to take part and complete the survey? Please write as many as possible:

This is the end of the questionnaire. Thank you for answering these questions!

☐If you are interested to spend 30 minutes for an interview, please tick the box!

The ORANGE Study: Online Research of Adolescents and Good Eating

Teenagers' Questionnaire (B)

DATE		ID NO.	

Hello! Thanks for taking part in the ORANGE Study. We would like to know a bit more about you. Fill in the boxes or tick the boxes.

Section 1. General Information

1.1 What is your date of birth? Day ☐ Month ☐ Year ☐

1.2 How tall you are?

☐ feet ☐ inches **OR** ☐ cm **OR** ☐ I don't know

1.2.a When was the last time you had your height measured?

☐ In the last month ☐ 1-6 months ago ☐ More than 6 months ago

1.3 How much do you weigh?

☐ Stones ☐ inches **OR** ☐ kg **OR** ☐ I don't know

1.4.a When was the last time you had your weight measured?

☐ In the last month ☐ 1-6 months ago ☐ More than 6 months ago

Section 2. Information about your lifestyle related to blood pressure

In this section, you will be asked about your lifestyle including physical activity, smoking, and alcohol intake. Please remember all of your answers will be kept confidential - please give honest answers.

Part 1. Physical activity

In this part, you will be asked about your physical activity in the last week ending yesterday.

2.1 Firstly, think about time you spend sitting, it includes studying, reading, using a computer, playing video games, watching TV, etc. both at school and out of school. Do not include sleeping time.

⇒ On a typical school day, how many hours do you normally spend sitting?

☐ hours/day

⇒ **2.1.a** On a typical weekend day, how many hours do you normally spend sitting?

☐ hours/day

Please think about the time you spend walking. 'Walking' here means walk at a normal speed, and at least 10 minutes. For example, if you walk fast for exercise, it should be counted in the next question. Another example is, if you walk from home to school, and it's more than 10 minutes, it counts; but if you walk from your bedroom to the kitchen for just few steps, it doesn't count.

2.2 On average, how many times a day do you walk? ☐

2.3 On average, how long do you spend walking each day? (Please think about the whole day) ☐ minutes/day

Now, please think about time you have spent on moderate intensity activities. They are activities when you can feel your heart beating a bit faster than normal, such as dancing, fast walking (which was not included in the previous question), slow cycling, etc.

2.4 In the last week, how many days have you done moderate intensity activities? ☐

2.5 On these days, normally, how long have you spent on moderate intensity activities per day? Please write the average minutes for one day. ☐ minutes on average

Finally, please think about the time you spent on vigorous intensity activities. They are activities when you are breathing rapidly and your heart is beating really fast, such as running, fast cycling, walking/climbing up a hill, playing football, basketball or volleyball, aerobics, etc.

2.6 In the last week, how many days have you done vigorous intensity activities? ☐

2.7 On these days, normally, how long have you spent on vigorous intensity activities per day? Please write the average minutes for one day. ☐ minutes in average

Part 2. Smoking

2.8 Which one of the following best describes you?

- ☐ I smoke every day
- ☐ I smoke occasionally, but not every day
- ☐ I used to smoke every day, but do not smoke at all now
- ☐ I have never smoked

If you currently smoke or used to smoke, please answer question 2.9 – 2.12

2.9 On average, how many cigarettes do/did you usually smoke each day on weekdays? ☐

2.10 On average, how many cigarettes do/did you usually smoke each day on weekends? ☐

2.11 How many years have you been/used to be smoking every day? ☐ years & ☐ months

2.12 If you have stopped smoking for what period of time have you been a non-smoker?

☐ half year or less ☐ more than half year but less than 1 year ☐ over one year

Part 3. Alcohol consumption

2.13 How often, if ever, do you drink alcohol?

☐More than once a week ☐Once a week

☐Less than once a week ☐Never drink alcohol

If you currently drink or used to drink, please answer question 2.14

2.14 Did you drink last week? ☐Yes ☐No

2.15 In a typical week, how much do/did you drink?

Alcopop, such as Hooch, Bacardi Breezer, WKD or Smirnoff Ice ☐ glasses each week

Beer, larger or Cider ☐ cans each week

Wine, including prosecco and champagne ☐ glasses each week

Sherry or fortified wine, such as port, cinzano, vermouth) ☐ glasses each week

Spirits, such as cocktails, vodka, rum, etc. ☐ glasses each `week

Section 3. Your knowledge and experience of blood pressure

3.1 Have you ever had your blood pressure measured?

☐Yes ☐No ☐I don't know

3.2 Has anyone ever told you that you have high blood pressure?

☐Yes ☐No ☐I don't know

3.3 Does anyone in your family have high blood pressure?

Your mother has high blood pressure ☐Yes ☐No ☐I don't know

Your father has high blood pressure ☐Yes ☐No ☐I don't know

Your brother or sister has high blood pressure ☐Yes ☐No ☐I don't know

Your grandfather or grandmother has high blood pressure ☐Yes ☐No ☐I don't know

Section 4. Your diet habits

4.1 Would you describe yourself as a vegetarian? ☐Yes ☐No

4.2 How often do you add salt to any food at the table?

☐Always ☐Usually ☐Sometimes

☐Rarely ☐Never

Please estimate how often you have eaten the following food in the last 3 month, and tick in the box that best describes your dietary habits.

Foods	Never	Once per month or less	2~3 times per month	Once per week	2~6 times per week	Once per day	2~3 times per day	3+ times per day
Milk								
Red Meat (e.g. beef, port, lamb)								
Fish								
Beans								
Fruit								
Vegetables								
Nuts								
Fat spread								
Salty snacks								
Sweets & Chocolate								
Take away ready meal								
White bread								

Section 5. Your family

5.1 Please select the best description that describes your ethnic background

☐White ☐Mixed ethnic group ☐Black or Black British

☐Asian or Asian British ☐Any other group, please specify: _____ ☐I don't know/I don't want to answer

5.2 Your mother's current job is _____ ☐I don't know

5.3 Your father's current job is _____ ☐I don't know

5.4 If you are living with a guardian but not your parents,, his/her current job is _____ ☐I don't know

This is the end of the questionnaire. Thank you for answering these questions!

JOIN US !

Hello! Welcome to the ORANGE Study: Online Research of Adolescents and Good Eating.

As people are moving their life online, why don't we also move the scientific research online?

Few people are exploring the possibility of moving the health research online. Therefore, we are inviting YOU to join our ORANGE study, the first online health survey among teenagers in UK, or maybe even in the world.

Imagine that few years later, it might be commen for health scientists to do survey online- it will save lots of time and expenditures for the scientists, and is easier for the participants as well. At that time, all of these scientists will own you a big thanks for your contributrion here in the ORANGE Study!

Join us and join the first group of teens who conduct health research online! This is SO COOL!

If you are interested in being one of the cool guys, please select which button suits you.

Appendix 15: The ORANGE study website

If you are a teenager 16 years old and over, and...

- you want to join the study now, please click the red button and read more about the study

I WANT TO JOIN NOW!

- you want to think about it and then decide, please click the grey button and leave your email address on the popping out page, we will contact you soon!

LET ME THINK ABOUT THAT

If you are under 16 years old,

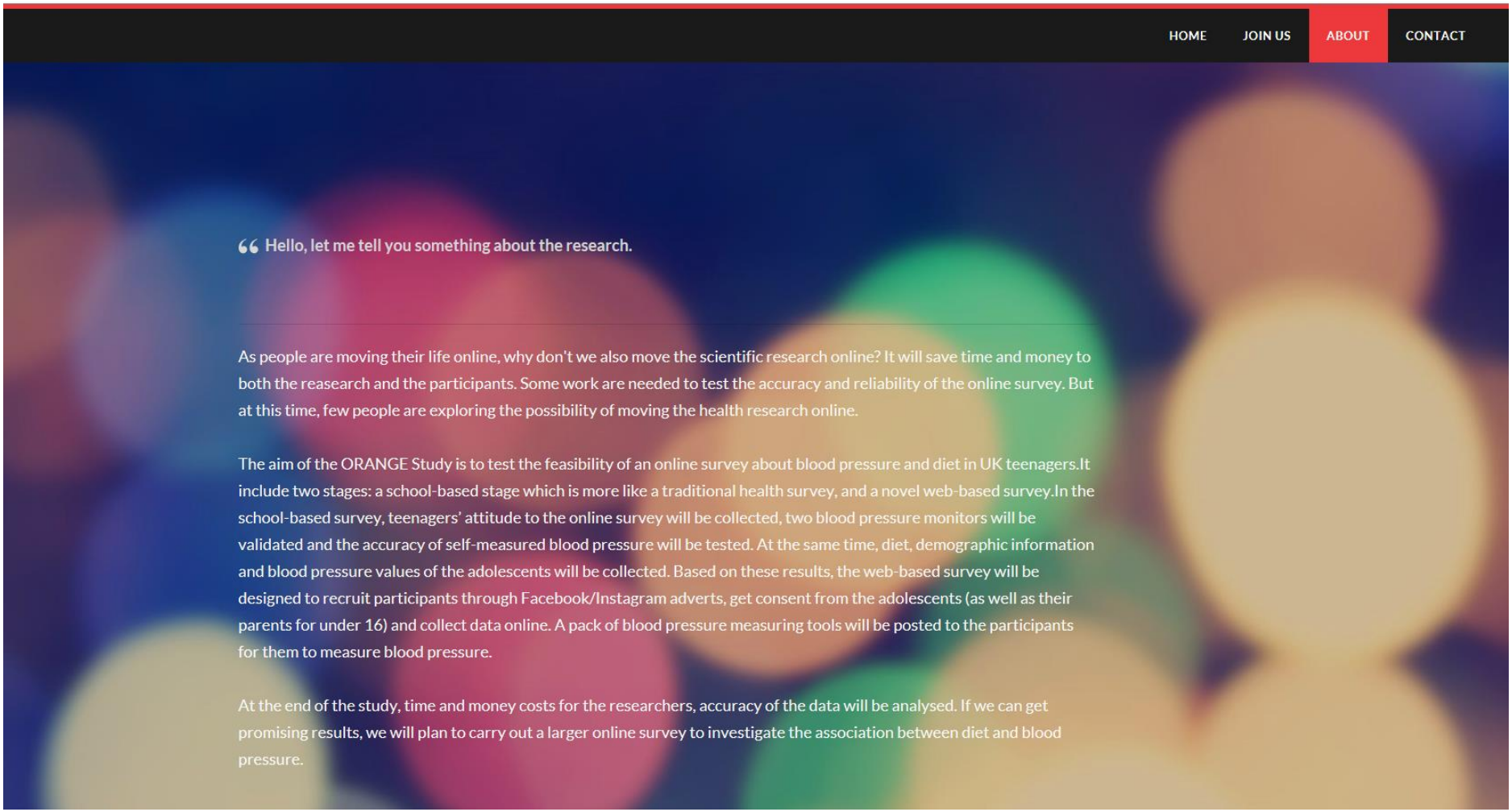
we will need your parents to give consent to us, please click the red button, enter your email address, your parents' email address on the popping out page. We will contact you and your parents soon!

I'M UNDER 16

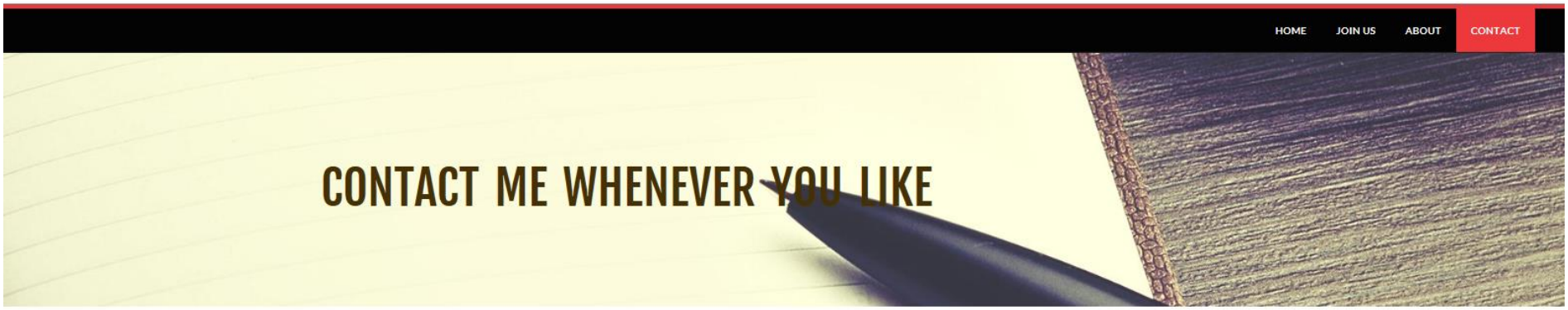
If you are a parent,

we wish you to leave the email addresses of you and your child. We will contact both of you soon! We will need your consent if your child is under 16 years old.

I'M A PARENT



Appendix 15: The ORANGE study website



Contact Me

I'm looking forward to hear from you. Let me know your feedback and any comments!

Please contact me through these three ways listed on the right.

Remember to include your Survey ID when get in touch with me!

Follow me on Facebook

Orangestudy Uol

Send me an Email

fszl@leeds.ac.uk

Write me a mail or come to find me in Leeds :)

Room G.07
Food Science Building
University of Leeds
Leeds
UK
LS2 9JT

Table 16.1 Strategy to post adverts on Facebook and Instagram of the ORANGE study

Round	Budget (Pounds)	Budget type	Duration (Days)	Term/Holiday
1	3.0	Lifetime	1	Term
2	11.2	Lifetime	3	Term
3	24.0	Lifetime	3	Term
4	12.2	Daily	7	Mid-term holiday
5	20.0	Daily	7	Mid-term holiday
6	20.0	Daily	10	Mid-term holiday

Join the **ORANGE** Study,

spend 1 hour with us then

have your diet analysed for

FREE and **get £5 voucher**

Organised by the University of Leeds