CHAPTER 1

General introduction
DIETARY INTAKE AND PHYSICAL ACTIVITY

Lifestyle and health
Dietary intake and physical activity are ever-recurring daily lifestyle behaviours. Dietary intake refers to all foods and beverages a person consumes. Dietary intake can be assessed as the amount of energy consumed, also referred to as diet quantity, and as the accordance with dietary guidelines, i.e. diet quality. Physical activity can be defined as “any bodily movement produced by skeletal muscles that requires energy expenditure”. This definition includes more than physical exercise alone. It also refers to physical activity at work or school, physical activity while commuting, physical activity during household chores, etc. Both lifestyle behaviours are important for a person’s health and specifically for a person’s body weight: The amount of energy consumed and the amount of physical activity, together with the basal metabolic rate and the thermic effect of food, contribute to the energy balance. There is a certain day to day variation in energy balance, but in general the body should be capable to keep an equilibrium between “energy in” and “energy out”. An imbalance between energy intake and energy expenditure causes either weight loss or weight gain. Weight gain over a longer period of time can lead to overweight or obesity. Obesity is defined as “abnormal or excessive fat accumulation that presents a risk to health”. This health risk includes the increased risk of noncommunicable diseases (NCDs), such as cardiovascular diseases (CVDs), certain types of cancer, respiratory diseases and type 2 diabetes.

A healthy lifestyle is always important for a person’s health, but especially when a woman has the wish to conceive or is pregnant since a woman’s lifestyle before and during pregnancy not only affects her own health but that of her offspring too. Diet, body weight and physical activity are associated with fertility, e.g. obesity is associated with anovulation, irregular menses and infertility. Furthermore, the risk of pregnancy complications seems to decrease when consuming a more healthy diet and by being more physically active during pregnancy through the prevention of excessive gestational weight gain. Moreover, maternal lifestyle behaviours and body weight are associated with the development and growth of the foetus and later life health of the offspring.

Current lifestyle and body weight
The Dutch national food consumption survey showed that women of reproductive age consume on average 130 grams of vegetables per day and 95 grams of fruit per day (which equals 1 piece of fruit), while the Health Council of the Netherlands advises to eat at least 200 gram of vegetables per day and 2 pieces of fruit. Additionally,
they drink on average 336 grams of sugary drinks (more than 1.5 glasses per day), although the advice is not to consume sugary drinks. If we specifically look at women with an active wish to conceive, a Dutch study showed that around 70% of women planning a pregnancy exceeded the recommended daily allowance of energy intake and almost all women exceeded the recommended daily allowance of saturated fat intake. Additionally, fruit and vegetable intake as well as different micronutrient intakes (iron, selenium, copper) were below the recommended intake in more than half of the women. Furthermore, almost all women (96%) planning a pregnancy consumed alcohol and 20% of them smoked. Another Dutch study showed that around half of women with an active wish to conceive did not meet the recommended folate (50%), vitamin D (67%) and eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) recommendations (52%). Also food consumption data of other developed countries, like the United Kingdom and Australia, show that women of reproductive age do not meet the nutritional recommendations.

The Dutch physical activity guidelines are defined as being physically active at moderate to vigorous intensity for at least 150 minutes per week in combination with muscle and bone strengthening activities at least twice per week. In the Netherlands, only 44.3% of all women aged 18 years and older met the national physical activity guidelines in 2017. On average between 55-67% of the Dutch women aged 18-50 years participates weekly in sports. Furthermore, over the last years, sedentary behaviour at work and at home is more prevalent and there is an increase in the use of physically inactive modes of transportation.

The suboptimal dietary intake and decrease in physical activity contribute to the rising levels of obesity in general and also among women of reproductive age. In 2017, 7.6% of Dutch women aged 20-30 years and 12.8% of Dutch women aged 30-40 years old were obese. It is expected that the prevalence of obesity among women in the Netherlands will rise up to 22% in 2040.

**CHANGING DIETARY INTAKE AND PHYSICAL ACTIVITY**

The difficulty of changing lifestyle

The percentage of women not meeting the dietary and physical activity guidelines, combined with the rising obesity among women of reproductive age underline the need for intervening to improve lifestyle before the start of pregnancy. However, changing lifestyle and maintaining a healthy lifestyle in the long term are notoriously
difficult. Lifestyle interventions often result in modest short term lifestyle change, and maintenance of a healthy diet and regular physical activity in the years following lifestyle intervention is hard. For example, a systematic review, including eight randomised controlled trials, showed that people can make healthy dietary changes in the 6-12 months after the start of an intervention. Nevertheless, the intake of fat, fruit, vegetables and fibre returned to baseline levels after 12 months of follow-up.

Life changing events

Although changing lifestyle is difficult, it seems that a person is more susceptible for lifestyle change during specific moments in life, which are associated with increased perceptions of personal risk, increased emotions and redefining of social roles and self-concepts. These particular moments are also called “triggering events” or “teachable moments”. The period around pregnancy can be seen as such a moment: Besides their own health, future mothers feel responsible for the health of their expected child. A clear example is the number of women who quit smoking when wishing to conceive or during pregnancy. The willingness of women to improve lifestyle before conception was also illustrated in a recently published study, showing that 65% of eligible women were willing to postpone removal of their contraceptive implant or uterine device for 6 months to improve their preconception health.

Intervening during the preconception period

Interventions using pregnancy as the triggering event to change lifestyle are mainly focussed on the pregnancy period itself. Only few studies focussed on the preconception period and report changes in dietary intake and physical activity as an outcome. A Dutch study examined the effects of a tailored preconception counselling session in subfertile couples (N=110). They showed that women increased their fruit and fish intake, decreased their alcohol intake and were more physically active 3 months after the tailored counselling session.

Another study examined the effectiveness of a preconception intervention among fertile women, compared to women who did not receive any intervention (N=692). Although dietary intake itself was not measured, women allocated to the intervention group were more likely to report higher self-efficacy for eating a healthy diet, had a greater intention to eat healthier diets and were more likely to meet the recommended levels of physical activity compared to the control group. The 12-month follow-up of this study showed that non-pregnant women allocated to the intervention group had a lower weight and
BMI compared to non-pregnant women in the control group (N total=362; follow-up rate=52.3%).

Changes in lifestyle and women’s health
Not only is the period around pregnancy a window of opportunity to change lifestyle, pregnancy can also be considered an important stress test for women’s cardiovascular health. Women who start their pregnancy with an unfavourable lifestyle and being overweight or obese have a higher risk of developing pregnancy complications, which are associated with an increased cardiovascular risk later in life. For example, women who had preeclampsia during pregnancy have a 4-fold increased risk of future heart failure and a 2-fold increased risk of future stroke, coronary heart disease and cardiovascular death. It is therefore of great importance to stimulate a healthy lifestyle before pregnancy, aiming to begin pregnancy with a healthy body weight.

Lifestyle intervention programs among women of reproductive age indeed showed positive effects on cardiovascular risk factors such as body weight, markers of vascular inflammation, insulin resistance, blood pressure and lipid profile. Results of lifestyle interventions on cardiometabolic health are often studied as a randomised comparison between groups. However, the response to lifestyle interventions varies among individuals and this variation could affect cardiometabolic health. By studying associations of lifestyle and body weight changes with later life cardiometabolic health, more knowledge can be gathered about dose-response relationships between lifestyle and later health. This information will help to formulate lifestyle recommendations in primary prevention of obesity and cardiometabolic disease.

MATERNAL LIFESTYLE AND OFFSPRING’S HEALTH
The Developmental Origins of Health and Disease (DOHaD) hypothesis
There is a large body of evidence to suggest that chronic degenerative diseases originate in early life. In utero, the developing foetus adapts to its environment, which is also called developmental programming. These adaptations to the environment have lasting consequences for the structure and function of the organs and tissues developing at that time. This means that maternal dietary intake and physical activity around the period of pregnancy do not only influence women’s health, but affect offspring’s health too. Additionally, multiple observational studies showed that maternal obesity before and during pregnancy is associated with offspring overweight/obesity and more
adipose tissue, unfavourable metabolic health, higher blood pressure, and higher cardiometabolic risk.

A large body of evidence supports the hypothesis that maternal dietary intake plays an important role in programming offspring health. Animal studies showed that manipulation of maternal dietary intake before or during pregnancy affects offspring health. Furthermore, natural experiments like famine studies showed that maternal undernutrition during gestation is associated with later life risk factors for cardiovascular diseases, like impaired glucose tolerance, hypercholesterolaemia, high blood pressure and obesity. Additionally, multiple human studies showed associations between maternal dietary intake in pregnancy and offspring health, for example the positive association between maternal carbohydrate during pregnancy and offspring blood pressure.

Increasing maternal physical activity during pregnancy might be an early intervention to improve cardiovascular health of the offspring, as it is associated with reduced offspring heart rate, increased heart rate variability and altered vascular function. Additionally, physical activity in obese pregnant women improved offspring glucose homeostasis and metabolism. Moreover, animal research showed that increased maternal physical activity abolishes the harmful effects of in utero exposure to a high fat or protein restricted diet, suggesting a positive effect of restoring the energy balance by increasing physical activity to compensate for increased energy intake.

From pregnancy to the preconception period

Human research in the DOHaD field has focussed mainly on the effects of dietary intake and physical activity during pregnancy. The attention currently shifts to the preconception period, since there is increasing evidence that the early embryo is highly sensitive to its environment and most organs develop in very early pregnancy. Hence programming may occur from the earliest stages after conception. Indeed, several lifestyle trials that intervened in pregnancy, by aiming at avoiding excessive gestational weight gain, did not show the desired improvements in foetal and offspring health outcomes. This suggests that these lifestyle interventions were initiated after the early and most critical period of foetal development. To date, few preconception interventions followed women and their offspring over time to study the programming effects of maternal preconception lifestyle on offspring later life health.
AIM AND OUTLINE OF THIS THESIS

Research questions

Many women of reproductive age do not meet the recommended dietary intake and physical activity guidelines. Improvements in their lifestyle might have beneficial effects for their own health and the health of their offspring. It is difficult to change lifestyle, but teachable moments such as the period around pregnancy can be used as a trigger to change dietary intake and physical activity. Therefore, we aim to answer the following research questions:

1. Does a preconception lifestyle intervention change women’s dietary intake and physical activity?
2. Are the lifestyle changes after following a preconception lifestyle intervention sustainable over a longer period of time?
3. Is preconception dietary intake and physical activity associated with cardiometabolic health of women in the long term?
4. Is preconception dietary intake and physical activity associated with cardiovascular health of the offspring?
5. Based on the currently published evidence: Is there an association between dietary intake and physical activity of women before and during pregnancy with the blood pressure and vascular health of their offspring?

Hypothesis: a preconception lifestyle intervention improves lifestyle and cardiometabolic health of two generations

We hypothesised that the wish to conceive serves as a trigger to change preconception lifestyle, which favourably affects women’s lifestyle and cardiometabolic health in the long term. Moreover, a more healthy preconception lifestyle results in a healthier lifestyle and body weight at the start of pregnancy, which favourably affects cardiovascular health of the offspring. Therefore, we hypothesise that a preconception lifestyle intervention has the ability to improve health and lifestyle of two generations: women and their children.

LIFEstyle study and WOMB project

To answer our research questions, we used data of the LIFEstyle study. The LIFEstyle study was conducted between 2009 and 2014 and was the first large randomised controlled trial (RCT) studying the effects of a preconception lifestyle intervention in a large group of obese, infertile women on reproductive, gestational and delivery
outcomes. During the LIFEstyle study, women were four times asked to fill out a Food Frequency Questionnaire (FFQ) and the Short QUestionnaire to ASsess Health-enhancing physical activity (SQUASH). These questionnaires provided information about preconception dietary intake and physical activity of all women over a one year period (Figure 1.1). Around 3-8 years after randomisation into the LIFEstyle study, we contacted all women and their children, conceived within 24 months after randomisation, for follow-up on their lifestyle and cardiometabolic health. This follow-up study was called WOMB project, which is an acronym for Women, their Offspring and iMproving lifestyle for a Better cardiovascular health of both. The WOMB project consisted of two stages, during which we collected detailed information about current lifestyle and cardiometabolic health of both women and children.

**Figure 1.1** Flow-chart of the LIFEstyle study and WOMB project. X=data collection point used in this thesis.

**Contents of this thesis**

This thesis is divided into two parts: Chapters 2-4 describe the effects of a preconception lifestyle intervention on women’s lifestyle and cardiometabolic health, and chapters 5 and 6 describe the effects of maternal lifestyle around the period of pregnancy on offspring’s cardiovascular health. Chapter 2 describes the effects of a preconception lifestyle intervention on dietary intake and physical activity during and six months after the intervention period (research question 1). In chapter 3, the long term effects of this same preconception intervention on dietary intake and physical activity are described (research question 2). If changes in dietary intake, physical activity and body weight during the first six months of the LIFEstyle study led to a better cardiometabolic health of women 3-8 years after randomisation is described in chapter 4 (research question 3). Cardiometabolic health outcomes were defined as BMI, blood pressure, body composition, pulse wave velocity, glycaemic parameters and lipid profile.
Chapter 5 describes if preconception dietary intake and physical activity is associated with offspring’s cardiovascular health (BMI, waist:height ratio, blood pressure, body composition and pulse wave velocity) at age 3-6 years old. Chapter 6 presents a systematic literature review summarizing evidence that examines the association between maternal dietary intake and physical activity before and during pregnancy with offspring’s cardiovascular health.

An overview of the main findings accompanied by a critical discussion on methodology and results is reported in chapter 7. This chapter also provides recommendations for future research and public health.
REFERENCES


GENERAL INTRODUCTION


