CHAPTER

Synthesis


Chapter 1

1.1 WHY SHOULD WE STUDY CHILDLESSNESS?

In many Western countries, childlessness has been increasing over the last decades (Miettinen, Rotkirch, Szalma, Donno, & Tanturri, 2015). For example, in the Netherlands, among women born in 1940 only 12% remained childless, while since the birth cohort of 1955 more than 17% remained childless (Human Fertility Database, 2017a). In the US, childlessness increased especially between women born between 1940 and 1960, with childlessness rates going up from 7.5% to 16%, after which these levels dropped to 13% among women born in 1970 (Human Fertility Database, 2017a). In Sweden around 11% of women born around 1940 remained childless, this was around 14% for the women born around 1960 (Persson, 2010). More recently in Sweden the childlessness rates seem to be dropping again to around 12% among women born in 1970 (Human Fertility Database, 2017a).

An important distinction to make when discussing childlessness is the one between desired and undesired childlessness. This distinction, however, is not as straightforward as it sounds. Some women and men are certain that their childlessness is undesired because they had a very strong desire to have children, which remained unfulfilled. Others are very certain that their childlessness is desired because they had no desire whatsoever to become a parent. However, there is likely a group of individuals who might not have had very strong preferences, or who changed their preferences over the life course and thus do not strongly identify with either voluntary or involuntary childlessness. For this reason voluntary and involuntary childlessness could be seen as a continuum (Letherby, 2002) (See Box 1 for further elaboration on measurement of voluntary and involuntary childlessness).

It is likely that the high levels of childlessness observed nowadays are not solely driven by increases in the group of men and women who have no children by choice, because the proportion of men and women who desire to remain childless is substantially lower than the proportion of men and women remaining childless. Moreover, the desire to remain childless increased only slightly in prevalence over the last decades (Miettinen & Szalma, 2014). Also, during the same period in which childlessness increased, the age at which people attempt to have their first child also increased, which is related to increases in involuntary childlessness (te Velde, Habbema, Leridon, & Eijkmans, 2012). Thus, a substantial fraction of the current high levels of childlessness is (probably) involuntary, which is associated with lower well-being (McQuillan et al., 2012) (see section two of this synthesis for a more elaborate overview of consequences of childlessness).

Much previous research has focused on what causes people to remain childless. This research can be broadly divided into three parallel strands of research. A first strand of research, typically from within the social sciences, has examined socio-demographic factors, such as educational and occupational behavior, religion and the role of the social network

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1 The last cohort for which we report childlessness levels, are women born in 1970, because women born in later cohorts did not yet reach the age of 45 and thus for them childlessness might not be lifelong childlessness.
underlying fertility behavior. Medical research is a second strand of research that has focused on which diseases or deficits cause fecundity problems. The third strand is the growing body of research which has focused on the genetic factors related to fertility (outcomes). These three strands of research have mainly been examined in isolation, although some attempts have been made to bring them together (for example by Briley et al. 2017; Tropf and Mandemakers 2017). Several gains can be made when examining these factors simultaneously: firstly, we can examine the relative importance of genetic risks versus social factors; secondly we can examine whether the influence of genetic factors is dependent upon environmental influences, and; thirdly we can examine how social and genetic factors relate to each other. For these reasons, in this dissertation I study genetic and socio-environmental factors underlying childlessness jointly within a sociogenomic approach. In Figure 1, a conceptual model on factors that influence childlessness that will be considered within this dissertation, is depicted.

Figure 1 | Conceptual model outlining hypothesized effects and interrelationships between factors causing childlessness. We hypothesize correlations between socio-demographic and genetic factors (the double sided arrow). We hypothesize a direct effect of sociodemographic factors on childlessness as well as an effect of socio-demographic factors mediated by postponement of childbearing and fertility desires. We hypothesize direct effects of genetic factors on childlessness as well as interactions between genetic factors and socio-demographic factors and genetic factors and the mediation factors.

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2 Fertility and fecundity can have different meanings in different research fields. For the purpose of this synthesis, fertility is defined as the number of children that people have and fecundity as the physiological ability to have children. Infertility is defined as the physiological inability to have children.
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Box 1 Measurements of involuntary and voluntary childlessness

In previous research, the distinction has been made between those who are voluntary childfree and those who are unable to have children (Bloom & Pebley, 1982). In some studies involuntary childlessness is still defined as only those with fecundity problems (Abma & Martinez, 2006; Avison & Furnham, 2015; Martinez, Daniels, & Chandra, 2012; Tanturri & Mencarini, 2008; Waren & Pals, 2013). However, many women who are initially able to have children voluntarily postpone childbearing until they reach an age in which it is difficult or socially less accepted to have children, which could be considered voluntary postponement but involuntary childlessness (Rowland, 1998). In other studies the group of voluntary childless individuals is divided into two groups, those that are "early articulators", who already at a young age state the desire to remain childless, and the "postponers", who revise their fertility desires during the life course (Houseknecht, 1979). In yet other studies three groups of childless individuals are described, the "traditional group" which is childless because of biological fecundity issues, the "transitional group" which is ambivalent and more career oriented, and the third group called the "transformative-childfree group" that has a strong desire to remain childfree (Ireland, 1993). In this categorization the transitional group lies in between the voluntary and involuntary childless individuals. Yet more types of childless individuals have been proposed in other research, for example, people who remain childless because they do not have a partner, those who have a partner who does not want to have children, or those who postpone childbearing until it is too late to have children (Graham, Hill, Shelly, & Taket, 2013).

Another way to distinguish between voluntary and involuntary childlessness might be simply asking individuals whether they are voluntary or involuntary childless. However, a reason to interpret answers on voluntary and involuntary childlessness with caution is that people generally would like their behaviour and beliefs to match. Men and women who do not have children might feel more comfortable with the idea that they actually never wanted to have children than with the feeling of regret of remaining childless. For this reason individuals would over-report voluntary childlessness because otherwise their status would not match their beliefs (Mcquillan, Greil, Shreffler, & Tichenor, 2008). Longitudinal studies furthermore indicate that individuals often change their opinion from wanting to have children to not wanting to have children and vice versa (Heaton, Jacobson, & Holland, 1999), supporting the argument that there is no clear distinction between voluntary and involuntary childless individuals.

Due to the difficulties in distinguishing between voluntary and involuntary childlessness, in the studies of this dissertation we do not make a distinction between voluntary and involuntary childlessness. However, when referring to voluntary childlessness we mean remaining childless while not having had the desire to have children, and not merely remaining childless in the absence of fecundity problems.
In this synthesis I will first elaborate on the consequences of remaining childless, then give an overview of important previous findings on why people remain childless, and supplement this with the new findings from this dissertation. I will start with focusing on the social factors that are related to remaining childless, and more specifically examine two important reasons why these factors result in childlessness, namely through desires to remain childless and through postponement of childbearing. Subsequently, I will go into the biomedical factors related to remaining childless and related to this the genetic factors associated with childlessness. Finally, I will look at the relation and interaction between social and genetic factors.

1.2 CONSEQUENCES OF REMAINING CHILDLESS

1.2.1 Consequences of involuntary childlessness
Although I realize that the distinction between voluntary and involuntary childlessness is not clear cut, many studies focused specifically on the consequences of involuntary childlessness and found some negative consequences (McQuillan et al., 2012). This is likely because involuntary childless women\(^3\) (in this case those who are not able to conceive) often feel regret for not having children and more often experience sadness related to their childlessness (Jeffries & Konnert, 2002; McQuillan et al., 2012). Involuntary childlessness due to the inability to have children is associated with a large range of negative outcomes, such as symptoms of anxiety, depression and grief (Lechner, Bolman, & van Dalen, 2007), lower quality of life and lower relationship satisfaction (Monga, Alexandrescu, Katz, Stein, & Ganiats, 2004), lower levels of well-being and life satisfaction (Callan, 1987; Jeffries & Konnert, 2002) and a higher chance to develop psychiatric disorders (Baldur-Felskov et al., 2013).

1.2.2 Consequences of childlessness
With regard to the distinction of childless individuals (voluntary and involuntary combined) with those who became parent, it is commonly believed that having children is beneficial for well-being (Hansen, 2012). Reasons for this belief is that it is assumed that children bring a sense of meaning to life, that having children results in great enjoyment and that having children increases marital happiness (Hansen, 2012).

The empirical results on the effects of childlessness on wellbeing are however ambivalent. On the one hand there are some studies that indeed report that having children has positive consequences for an individual’s well-being. For example, a study in Australia found that during reproductive years, between age 25 and 44, childless women experienced lower well-being (Graham, 2015). A different study found that having a first child positively effects well-being, especially for women with traditional family orientations (Balbo & Arpino, 2016).

\(^3\) We refer here to women, because most of the research on the consequences of childlessness mainly focuses on women.
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In Norway it was also found that having children has a positive effect on well-being for women (Kohler, Behrman, & Skytthe, 2005) and that childless women experience lower life satisfaction and lower self-esteem than mothers (Hansen, Slagsvold, & Moum, 2009).

Contrary to these findings of the positive consequences of having children there are also a number of studies that indicate that remaining childless might actually result in higher well-being. One reason for the positive effects of remaining childless might be that those who are childless report that they have more time and flexibility in life to spend on leisure activities and relaxation (Callan, 1987). Having children is also likely to result in work-life stress, which often results in lower well-being among those with children (Umberson, Pudovska, & Reczek, 2010). A large study that uses data from the World Value Survey shows that individuals without children are generally happier and report higher life satisfaction (Hansen, 2012).

The discrepancy in previous research likely arises because in some countries and time periods having children is more difficult to combine with other aspects of life, such as working, and therefore results in lower well-being, while in other countries having children can be combined more easily with other life aspects. This is supported by the findings that having children results in higher well-being especially in the Scandinavian countries where there is good support for parenthood (Aassve, Goisis, & Sironi, 2012; Aassve, Mencarini, & Sironi, 2015) and by findings that in Germany in more recent years, where women are more able to combine having a family with working, having children positively relates to well-being (Preisner, Neuberger, Posselt, & Kratz, 2018). The negative effect of childbearing on wellbeing is especially clear in the US where there is little family support policy (Hansen, 2012). On the individual level it is also found that having children only results in lower well-being in the presence of work-family conflict (Matysiak, Mencarini, & Vignoli, 2016).

Among men the relationship between childlessness and well-being is possibly not as strong as for women. For example, for men it is found that it is not childlessness per se, but childlessness in combination with being single resulting in lower well-being (Dykstra & Keizer, 2009; Kohler et al., 2005).

The consequences of childlessness vary at different age levels. Although childless older individuals are not necessarily more often lonely (Zhang & Hayward, 2001), it is found that they often have smaller support systems (Tanturri et al., 2015) and lower life-satisfaction (Hansen, 2012). Due to their smaller support systems older individuals without children receive less social support than parents and are more likely to receive professional care or live in a nursing home (Albertini & Mencarini, 2014; Koropeckyj-Cox & Call, 2007; Michaela Kreyenfeld & Konietzka, 2017).

In conclusion, how childlessness and well-being are related is not entirely clear. The presence of work-family conflict is likely to suppress the otherwise positive consequences. Furthermore, the increasing levels of childlessness in combination with overall lower number of children that are born and a higher life expectancy results in a changing age composition of society (Sleebos, 2003). It is expected that the old age dependency ratio, which is the population aged 65 and over relative to the population between 15 and 64 years of age, will double between 2000 and 2050 (OECD, 2008) and therefore in 2050 there are only two 15-64 years olds to every 65+ year old. This changing old age dependency ratio will have consequences for the affordability of our pension system amongst others (OECD, 2008).
1.3 SOCIAL FACTORS UNDERLYING CHILDLINESS

The number of children people have and the age at which people have their first child are topics that are well-studied within the sociological and demographic literature. Childlessness has received considerably less attention, but even on this topic a substantive body of knowledge exists. The role of social factors examined within the field of sociology can be divided into three strands of literature: i) the macro level including institutional and cultural factors influencing childlessness, ii) the meso level including in particular socio-environmental factors influencing why people have children or not and iii) the micro level including individual characteristics related to remaining childless. The most important findings are discussed in the following sections.

1.3.1 Institutional and cultural context in Western countries

Institutional and cultural country contexts could have an influence both on the desire to remain childless as on the outcome of remaining childless though constraints. In many European countries as well as in the US there is a substantial gap between the intended and actual number of children that people have and a large gap exists between the proportion of people intending to remain childless and actually remaining childless (Beaujouan & Berghammer, 2017). For example, in the Netherlands only 7% of the 25 to 29 year olds intend to have no children, while at age 40 around 17% of them remain childless (Beaujouan & Berghammer, 2017). Similarly, in the US only 6% desired to remain childless while 13% ultimately remained childless (Beaujouan & Berghammer, 2017). This shows that the proportion of people who desire to remain childless do not fully explain the high rates of individuals remaining childless.

In most countries most people still would like to have children; when examining men and women in Europe under the age of 24, only 5% of the women and 10% of the men intend to have no children (Sobotka & Testa, 2008). Furthermore, there seems to be a persistent two child norm, with most individuals preferring to have two children. Between 1980 and 2010, there has only been a small decrease in the average ideal family size in Europe, dropping from 2.5 children desired in 1980 to 2.2 in 2010 and the proportion of women who report an ideal family size of none or only one child increased only from 5% in 1980 to 11% 2010 (Sobotka & Beaujouan, 2014). Corroborating evidence comes from a different study that examined the proportion of European individuals who intend to have no children at all which reported that between 2001 and 2011 there has been no increase in this intention (for men going from 9.1% in 2001, to 8.4% in 2006 to 9.1% in 2011, and for women going from 6.1% in 2001, to 6.9% in 2006 to 7.0% in 2011) (Miettinen & Szalma, 2014).

Studies that examine how cultural and institutional factors influence fertility generally focus on fertility outcomes and not on desires. One way in which the society people live in can shape fertility, is by determining how well men and women can combine work and family through work family policies and by setting the norms and values regarding desired family behavior. Previous research finds that when childcare is widely available, accepted and affordable, fertility rates are generally higher (Mills, Rindfuss, McDonald, & te Velde,
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2011) because it allows women to combine work with having a family. Also other work-family arrangements that allow women to combine work and family, such as the option to work flexible work hours, increase fertility rates (Harknett, Billari, & Medalia, 2014).

Religiosity, female labour force participation and divorce rates, that can be considered normative and cultural aspects, have typically been associated with fertility. It used to be the case that in countries with many religious individuals, low female labour force participation and low divorce rates, fertility rates were higher (Castles, 2003). However, these relations switched around completely between 1980 and 1998, with lower fertility in most Catholic countries and in countries with lower female labour force participation. This is probably because in countries with high female labour force participation policies that allow combining work and family were implemented. Related to actual findings on female labour force participation, show findings with regard to gender role attitudes on female employment a u shaped pattern with fertility, with high fertility in both the most traditional and most modern countries, for the same reason that in the most modern countries policies are implemented that allow the combination of work and family (Arpino, Esping-Andersen, & Pessin, 2015).

The previously research focuses on the number of children people have, however, in countries in which people have more children on average, the number of people who remain without children are not necessarily low. For instance, in Europe, no clear relationship between the two indicators of fertility is found (Prag et al., 2017) and also the US is characterized by relatively high levels of fertility as well as high levels of childlessness (Human Fertility Database, 2017a). Therefore, it comes as no surprise that some of the institutional factors that influence average number of children born do not strongly influence childlessness levels. Findings with regard to family support environments show that, for example, the flexibility of working hours, perceived job mobility and country expenditure on families have a stronger impact on second and higher order births than on first birth probabilities (Harknett et al., 2014). Unfortunately, very few studies specifically examined how institutional and cultural factors relate to rates of childlessness (Tanturri et al., 2015).

One normative factor that particularly relevant here is the approval of voluntary childlessness, which differs a lot across countries, from 84% of the people approving voluntary childlessness in Denmark, to 16% in Russia (Eicher et al., 2016). In less religious countries, richer countries and more gender equal countries this acceptance is generally greater (Eicher et al., 2016). In countries where the approval is greater, childlessness levels also seem to be higher.

Not only the national context, but also the regional context might influence fertility, as men and women living in cities generally have fewer children and are more often childless than men and women who live in rural areas and small villages (Kulu, 2012). Probably because of the higher costs to have children in a city, such as higher housing prices, and possibly also due to more traditional norms and values in villages compared to in cities.

1.3.2 Socio-environment: partnership trajectories, social network, social capital
In addition to the broad country level the direct social context, consisting of social relations, also influence individuals’ fertility behavior. The most important social relationship is whether
people have a partner (either married or cohabiting) during their fertile period (Keizer, Dykstra, & Jansen, 2008). Being married is still the most common union in which children are born, but large differences between countries exist (Sobotka & Toulemon, 2008). In Sweden 45% of the children are born to non-married cohabiting couples, in the US this is only 11% and in Poland only 2%. Whether the partner wants to have a child is also very important for the decision to have a child, although the desire of the female partner is more important in decision making than the desires of the male partner (Testa, 2012).

A characteristic of the couple that has received much attention in recent literature is the division paid and unpaid labour. Couples with a more gender equal division of house work in combination with gender-equal attitudes are more likely to have a second or third child than couples with less gender-equal attitudes and division of labour (Aassve, Fuochi, Mencarini, & Mendola, 2015). In Norway, a country with high gender equality, gender equity of household tasks positively influences first births as well as subsequent births (Dommermuth, Hohmann-Marriott, & Lappegard, 2017).

Social relations beyond the couple can also influence reproductive decision making in several ways (Bernardi, 2003). For instance, the probability to have a child increases when individuals’ friends or siblings have children (Balbo & Barban, 2014; Balbo & Mills, 2011b) or when overall more people in their network have children (Lois & Arránz Becker, 2014). One of the reasons why having more people with children in the network results in higher fertility (desires) is argued to be social learning: those with more friends and acquaintances with children in their network more often observe positive experiences related to parenthood (as it is assumed that the negative consequences of childbearing are well-known to everyone), which increase their fertility desires (Lois & Arránz Becker, 2014). Another reason could be the decreasing social opportunity costs, because people with more parents in their network expect less negative effects of having a child on their social contacts (Lois & Arránz Becker, 2014).

Social contacts could also serve as support when raising children, and therefore it is expected that individuals with larger social networks expect more support and for this reason would have more children. However, results are mixed in this regard. Phillipov and colleagues (2002) found indeed that individuals with greater support networks have higher fertility intentions. In contrast, other studies did not find that men and women who expect more social support are more likely to have a child (Kuhnt & Trappe, 2016), or that only emotional support and not practical support increase the chance to have a second or third birth (Balbo & Mills, 2011a). In the contrary, one previous study even found that having a very strong family network, which could work as a support system, decreases fertility intentions (Balbo & Mills, 2011b). Another way in which social contacts might influence fertility, is that people might perceive social pressure from their environment, and men and women who think that their parents, friends and family expect them to have another child more often have another child (Balbo & Mills, 2011a; Barber, 2000; Kuhnt & Trappe, 2016; Lois & Arránz Becker, 2014). Another influence of the social network is that men and women with more siblings have more children themselves (Booth & Kee, 2009) which might be due to social learning, which is that individuals copy the family behavior they are familiar with,
through intergenerational transmission of values, or through genetic influences on fertility (desires) (Barban et al., 2016; Bras, Bavel, & Mandemakers, 2013; Rodgers, Kohler, Kyvik, & Christensen, 2001).

1.3.3 Individual characteristics and childlessness
As described earlier, the national contexts in which people live, as well as their social contacts are likely to influence fertility decisions and outcomes. Of course, different individuals can vary in numerous characteristics. In the following sections we will address those individual level characteristics that are most commonly associated with fertility preferences and outcomes, including religiosity and ethnicity, education and labour force participation. People also differ in their biological capabilities to have children which will be addressed in part three of this synthesis.

Men and women who are more religious less often are childless because religion generally relates to traditional family values and values in favor of childbearing (Hayford & Morgan, 2008). In the US, religion is an important predictor for normative differences in reproductive behavior, with Catholic and Protestant women on average having more children (Frejka & Westoff, 2008). In Europe religion plays a less central role in the lives of many people, especially in West and Northern Europe, and although also in Europe women who consider religion more important have more children, the effects of religion are weaker than in the US (Frejka & Westoff, 2008).

Ethnicity is another important predictor of fertility; in the US there are marked differences in childlessness levels, with approximately 21% of the non-Hispanic white women remaining childless, 17% of the black women and 12% of the Hispanics (Carlson, 2015). These differences are partly because Black and Hispanics are more often from lower socio-economic background, where fertility is higher, but also due to differences in values and desires. Also in Europe the fertility rate of migrants is often higher than that of the native population (Kulu & González-Ferrer, 2014).

Some of the most often studied and most important factors related to childlessness are the educational and occupational behavior, especially of women. Because the relationship of education and occupation with childlessness is an important part of this thesis, I will examine these factors more in detail in the following paragraphs, describing the observed relationship and discussing the possible mechanisms that underlie this relationship.

Educational and occupational behaviour and childlessness in women
The level of education women have is a fairly consistent predictor of their fertility, including childlessness. Generally women with higher education have fewer children and more often remain childless (Basu, 2002). Although over the last decades the effect of education on the number of children for women has declined, the effect of education on childlessness seems more consistent (Kravdal & Rindfuss, 2008).

Not only the educational level influences fertility outcomes but also the educational field plays a role in explaining whether an individual becomes a parent or not; among women educated in education and health, childlessness is lowest (J. M. Hoem, Neyer, & Andersson,
Among women educated in science, technology and social sciences, childlessness is higher and among women educated in arts, humanities and general fields of study, childlessness is highest. In fields of study where women are able to combine work and family, where the percentage of women is large and where traditional family values are prevalent, women are less often childless (Michelmore & Musick, 2013). Similar to the the field in which women are educated, also the occupational field of women influences fertility outcomes. Women in technical and economic jobs more often postpone having children than women in healthcare or teaching jobs (Begall, 2013). Generally speaking, occupations related to caring and interpersonal skills are often related to low childlessness and high fertility (Cooney & Uhlenberg, 1989; Martin Garcia, 2010; Strand, Wergeland, & Bjerkedal, 1996).

The labour market participation of women is also a strong determinant of fertility behaviour. Previous research indicates that compared to women who are not active on the labour market, those working part-time and even more those working full-time are less likely to become a parent (Brewster & Rindfuss, 2000). Furthermore, childbearing is often delayed among women with high earning potential or who experience recent job mobility (Begall, 2013). Women’s income furthermore leads to a later age of having children, having fewer children in total as well as remaining childless more often (Barthold, Myrskylä, & Jones, 2012; Caucutt, 2002; Stulp, Sear, Schaffnit, Mills, & Barrett, 2016). The effect of income on first births seems to be lower for black and Hispanic women than for white women (Stulp et al., 2016) and a study in Sweden actually finds that women with higher income are more likely to have a child (B. Hoem, 2000). Overall, working women, women with high status jobs and women with a stable career more often remain childless (Friedman, Hechter, & Kanazawa, 1994; Heaton et al., 1999; Keizer et al., 2008).

With regard to the characteristics of a job in which a women works, women who experience more time pressure in their job less often have the intention to have children, women who experience little freedom and autonomy in their work also less often have children and women in an occupational field with a low proportion of women have children at a later age (Begall & Mills, 2011). Finally, women who work non-standard working hours less often have children (Begall & Mills, 2011). A lower level of childlessness is also observed in female dominated fields (Begall & Mills, 2013; J. M. Hoem, Neyer, & Andersson, 2006b).

In summary, being higher educated and working more hours increase the chance of remaining childless for women while working in a social and caring occupation decrease the chance of remaining childless. Several mechanisms have been proposed to underlie this relationship between educational and occupational behavior and childlessness.

Educational and occupational behaviour and childlessness in women: three mechanisms

The first mechanism proposed to underlie the relationship between educational and occupational behavior and childlessness is that work and family preferences are fixed at a young age and influence educational and occupational as well as fertility behavior simultaneously. This argumentation is mainly based on Hakims preference theory (Hakim, 2002, 2003, 2006) that suggests that there are three groups of women: i) those who are
family oriented, ii) those who are career oriented and iii) those who prefer to combine work with having family (and are referred to as "adaptive"). These orientations influence future behavior and thus explain the relationship between occupational and fertility behavior. Especially some of the research on educational field and occupational field seems to be using this theoretical framework. They propose that the choice of educational discipline which leads to a particular occupational field can be seen as an indicator of preferences regarding future lifestyle, not only with regard to one's occupation but also with regard to childbearing (Bavel 2010; Oppermann 2012; Begal & Mills 2013) and that women who want to have children might select themselves into fields that more easily allow having children (J. M. Hoem et al., 2006b).

If fixed life preferences would be the main driver of the relationship between education, occupation and childlessness, we would expect that already at a young age there would be a relationship between fertility desires and occupational desires, and that this one set of preferences would explain the relationship between education, occupation and childlessness later in life. In CHAPTER 2 data from the National Longitudinal Study of Youth 1979 (NLSY79) is used that followed women in the United States throughout their reproductive life span. This study uses information on fertility desires and intentions and thus allows us to empirically test mechanisms underlying the relationship between education and occupation with remaining childless. Our findings in CHAPTER 2 showed little evidence for the idea that there was a fixed set of preferences explaining the relationship between educational and occupational behavior with childlessness. Our findings showed that women who desired to remain childless did not desire to have higher status occupations later in life. Furthermore, occupational desires did not influence fertility behavior and vice versa fertility desires did not influence occupational behavior.

The second mechanism that explains the relationship between educational and occupational behavior and childlessness proposes that through socialization occurring when pursuing education and while working, women's family preferences change and influence fertility outcomes. Within higher education, certain individualistic values are transmitted that are less aligned with traditional and religious beliefs that promote family over career, and such values are thought to decrease the preference to become a parent (Heaton et al., 1999; Lesthaeghe & Surkyn, 1988). Also with regard to the educational field it is suggested that women might be socialized within the educational field, with women in social and caring educations being more exposed to a traditional nurturing and caring image of women (J. M. Hoem et al., 2006b). Although not directly related to socialization per se, there is also literature that suggest that higher educated women with higher income potential might change their fertility desires due to the greater financial losses that they will experience when staying at home to care for their children (Ermisch, 1989). This could be another reason why women may change their fertility desires during their career.

Based on socialization theory we would thus expect that higher educated and working women would develop a weaker desire to have children, resulting in childlessness. Our results in CHAPTER 2 were not in line with these expectations. With increasing age, all women adjust their fertility expectation downwards, but this adjustment was not stronger for women
who were higher educated or working in high status occupations (*FIGURE 2A-E CHAPTER 2*). Also during the years in which higher educated women were still in education, and thus would be exposed to more egalitarian or individualistic values, no increase in the desire to remain childless or decrease in the desired number of children took place.

A third proposed mechanism for the association between educational and occupational behavior and childlessness, is that due to educational and occupational behavior women experience constraints on family formation, which leads to postponement which in turn results in involuntary childlessness. More highly educated women spend more time in school and the roles of being a student and being a parent are difficult to combine (Stycos & Weller, 1967). After finishing education, women who are more highly educated might first want to pursue a career and therefore postpone motherhood (Becker, 1981; Gustafsson, 2003). They postpone childbearing due to the incompatibility between paid employment and motherhood (Bernhardt, 1993); working outside the home and caring for children are both time consuming for women given the gender-based division of household tasks (Keizer et al., 2008) which makes these two roles difficult to combine. Also working in male dominated jobs is supposed to result in lower fertility because in these fields lower levels of work-family support is provided (Cook & Minnotte, 2008; Davis & Kalleberg, 2006).

Our findings in Chapter 2 were most in line with the postponement mechanism, which suggested that over the life course, higher educated and working women experience more constraints to having children and therefore postpone childbearing attempts eventually resulting in childlessness. We saw that most women who would eventually remain childless for a large part of their life had the intention to have children (*FIGURE 2A CHAPTER 2*). Also, higher educated women did not more often have the desire to remain childless around age 20. Where lower educated women and those working in low status occupations already had children at young ages, or expected to remain childless at young ages, higher educated women (falsely) continued to expect to have children in the future up to higher ages (*FIGURE 2B-E CHAPTER 2*).

Thus, even though higher educated women did not more often desire to remain childless, they were much more often childless by the age of 45. These findings indicate that work and family life are difficult to combine especially for women working in high status occupations and who work many hours a week. This is in line with previous research on postponement of childbearing, which showed that educational and occupational characteristics were indeed strong predictors for a later age at first birth (Mills et al., 2011).

*Educational and occupational behaviour and childlessness in men*

For men the effect of education on childlessness is opposite to the effect for women or much weaker; higher educated men on average have more children and lower educated men are more often childless (Fieder and Huber 2007; Kravdal and Rindfuss 2008; Nisén et al. 2013; Oppermann 2014; Parr 2010, *CHAPTER 2, additional information*). Also occupational effects on fertility behaviour are typically very different for men and women. When a man has a stable career he will have a smaller chance to remain childless (Keizer et al. 2008, *CHAPTER 2, additional information*). Also men with higher incomes on average have more
children and less often remain childless, while the opposite effect is true for women (Nettle & Pollet, 2008). Furthermore, when a man works non-standard working hours, couples more often have a second child because they need less childcare and can combine work and family life better (Begall, 2013). With regard to SES the effect for men is unclear and differs between countries; in the US there is no influence of male SES on childlessness (Waren & Pals, 2013), in the UK high status males are more often childless (Hakim, 2006) while in Italy the opposite is true (Tanturri, 2010). Only one study that I am aware of focused on the effect of educational field for men and found that it does not seem to matter for men (Oppermann, 2014), although our findings in CHAPTER 2, (additional information) suggest that men who are working in social and caring occupations remain less often childless than men working in other types of occupations. In conclusion, generally men who are higher educated and have a stable income and job are less likely to remain childless.

For men, being highly educated and having a good job and income are theorized to result in being a more attractive marriage partner and therefore is expected to result in having more children (Kravdal & Rindfuss, 2008). In CHAPTER 2 (additional information) the relationship between fertility desires and remaining childless among men across different educational and occupational groups is displayed. These findings seem to hint towards the idea that a part of the differences in childlessness levels by educational groups could be due to differences in the desire to remain childless, since those men who are remaining childless less often (the higher educated men who work in high status occupations) also seem to desire to remain childless less often. Also another study among men in the US found that higher educated men more often have the desire to become fathers (Kessler, Craig, Saigal, & Quinn, 2013). The differences in desires could be an alternative explanation for the relationship between educational and occupational behavior and childlessness among men that deserves attention in future research.

1.3.4 The role of fertility desires and expectations in remaining childless

These three previously mentioned proposed mechanisms differ in the extent to which they propose that higher educated and working women are childless because they desire to remain childless or because their circumstances push them into lives without children. It is important to make this distinction because voluntary childlessness generally has less negative consequences in terms of wellbeing than involuntary childlessness.

Our findings from CHAPTER 2 are contrary to the research on voluntary childlessness, in which it is often suggested that many higher educated women and women who are successful in their career are voluntary childless (Avison & Furnham, 2015; Martinez et al., 2012; Waren & Pals, 2013). The shortcoming of this previous research is that it often conceptualizes voluntary childless as being childless in the absence of medical barriers to have children (See Box 1 for an elaboration on measurement of childlessness levels). However, in our study many higher educated women are likely involuntary childless, because they desired to have a child for a long time. Although some of these women likely postponed childbearing attempts up to ages at which having children might be more difficult, and thus might fall in this category of involuntary childlessness, many will also have postponed up
1.3.5 Postponement of childbearing resulting in childlessness

In Chapter 2 on the role of educational or occupational behavior on childlessness, it is noteworthy that, regardless of education, much fewer women desired to remain childless than eventually remained childless (Figure 1 Chapter 2). Only 8% of the women who did not have children between the age of 18 and 22 desired to remain childless, while of this group eventually more than 20% did not have children by the age of 45. Figure 1 in chapter 2 shows that around age 30 almost half of the women who eventually remain childless still expect to have a child in the future. The same pattern appears among men in the US (Kessler et al. 2013, Chapter 2, additional information), with many men who eventually remain childless expecting to have a child for a large part of their life. This suggests that childlessness is often not expected, at least not at young ages, and is likely to be involuntary. This suggests that postponement is often to a predecessor of childlessness, and therefore it is noteworthy to draw extra attention to postponement of childbearing in this dissertation on childlessness.

It is argued that at least part of the increasing levels of childlessness across countries is due to postponement of childbearing, because in the same period in which a large increase in childlessness took place, a substantial increase in age at first birth also took place. For example, in 1970 the average age at which women had their first child was around 25 years, while in 2014 this was close to 30 years (Human Fertility Database, 2017a).

There are three main reasons why postponement of childbearing attempts may result in childlessness. A first reason is that men and women who are childless get used to their childfree lives and the benefits it has, such as greater individual freedom, and therefore no longer desire to become a parent (Buhr & Huinink, 2017). A second reason is that people postpone childbearing up to an age at which they consider it to be socially unacceptable to start a family. Indeed, as previous research found that there are social age deadlines after
which people are considered to be too old to have children, which is usually around 40 years of age for women and around 45 years of age for men (Billari et al., 2011). A third reason is that individuals postpone childbearing up to an age in which they are less likely to conceive and deliver a child.

As is commonly known, especially for women, but to a lesser extent also for men (Eisenberg & Meldrum, 2017), the ability to have children decreases with age. Findings from natural fertility populations (populations in which no deliberate attempts are made to limit family size) for example showed that only 2% of the married women had their last childbirth before the age of 20, and based on this the authors concluded that 2% of the women are unable to have children after the age of 20 (Eijkemans et al., 2014). This percentage increases exponentially with age, with only 4.5% before age 25, 7% before age 30, 12% before age 35, 20% before age 38, 50% before age 40, 90% before age 45 and 100% before age 50. Also research focused on age at marriage and remaining childless in natural fertility populations found that a higher age at marriage was related to a greater chance of remaining childless (Menken, Trussell, & Larsen, 1986).

Combining information on the increasing age at first birth, with information on the decline in the ability to conceive with age resulted in a method to estimate rates of voluntary versus involuntary childlessness (te Velde et al., 2012). Estimations from this method indicated that due to postponement the rate of involuntary childlessness doubled between 1970 and 2007. For example, in the Netherlands the percentage of all women who involuntary remain childless was estimated to be around 3% in 1970 and over 6% in 2007. Although the exact size of these estimates should be interpreted with caution, the idea that postponement of childbearing attempts goes hand in hand with increasing levels of undesired childlessness seems plausible. The reason why these findings should be interpreted with caution is because estimates of declining fecundity with age could be distorted by deliberate choices not to have children. Furthermore, estimates of declining fecundity in historical populations might not be completely applicable nowadays, due to greater fertility awareness which increases fertility, but larger obesity rates increasing infertility (te Velde et al., 2012). Furthermore, it would be unlikely that the negative effects of postponement of childbearing could be fully compensated by assisted reproductive technologies. However, even under the very optimistic scenario that 100% of the couples facing infertility would have access to ART there would still be an increase in involuntary childlessness, given that the effectiveness of assisted reproductive technologies also decreases with age (Leridon, 2004).

What is postponement?

Much of the previous research on the postponement of childbearing has focused on the age at which people have their first child rather than on postponement itself (Mills et al., 2011). However, as we find in Chapter 2, a large part of men and women who postpone childbearing eventually did not have a child and these “postponers” are thus ignored in previous research. I argue that to examine the postponement of childbearing, three facets need to be studies. First we should consider planned postponement, which is the age at which people would like to have their first child. Second, we should consider continued
postponement, which is the extent to which people adjust their desired timing of first birth over the life course. Third, we should consider if people have a child within their desired time frame or not. The combination of these three facets can give insights in the high ages at first birth observed as well as postponement leading to childlessness. It could furthermore shed light on the fluidity of childbearing intentions.

What influences different facets of postponement?

In Chapter 3 we study these three facets of postponement and examine influential factors. We use data from the Longitudinal Internet Study for the Social Sciences (LISS) which is a representative sample of the Dutch population. When it comes to the first facet, a striking finding is that Dutch men and women plan to have a child at rather high ages (averaging around 31) (Chapter 3, Figure 2A), and even if we look at men and women who are between 18 and 22, so for whom postponement of childbearing has probably not occurred yet, the desired age is over 29 (Chapter 3, Figure 2B). For comparison, when looking at the European Social Survey, the age that people consider ideal for men and women to become parent is 25.9, and even though this is somewhat higher in the Netherlands, around 27.3 (ESS, 2006, own calculations), this is still several years younger than the age at which people think they will become parents themselves. When we examine continued postponement, we find that many men and women adjust their planned timing to have a first child. Among those that were asked multiple times about their desired timing of their first child, approximately 34% lowered their desired age, 17% did not change their desired age at which they wanted to have their first child, and 49% increased the age at which they wanted to have their first child (see Chapter 3, Figure 3). Finally, when it comes to having a child within your desired time frame, only about half of the men and women have a child within their desired time frame (Chapter 3, Figure 4).

When we look at the factors that influence these three facets of postponement, we find that many practical considerations play an important role. Most important is whether an individual is in a relationship, with those who are married or cohabiting expecting to have their first child earlier than those who are single, and in between are individuals who are in a relationship and not cohabiting (Chapter 3, Table 2). Being single or breaking up is related to further postponing the age at which you plan to have a first child. Those who are in a relationship also more often had a child within their desired time frame and generally have a child earlier. Despite rather relaxed norms about marriage and cohabitation and low rates of marriage in the Netherlands, those who are married have a child earlier than men and women who are cohabiting. Perhaps because getting married is a consequence of the intention to have a child (Hart, 2015). Our findings on the role of relationship status and family formation are in line with previous research that finds that those in a relationship plan to have a child within a shorter time frame and also are more likely to realize these intentions (Berrington, 2004; Dommermuth, Klobas, & Lappegård, 2011).

An important factor that may cause the increasing age at first birth is the increasing educational attainment among women (Mills et al., 2011). Indeed, we also find that the higher educated plan to have a child at higher ages than the lower educated, which holds both for
men and women. However, we did not find that those who are higher educated are less likely to actually have a child within their desired time frame, also not when looking at men and women separately, and actually those who are medium educated are a bit less likely to have a child within their desired time frame (CHAPTER 3, TABLE 2 and 3). Also research from other European countries found that higher educated individuals are actually more likely to realize their short term fertility plans (Dommermuth, Klobas, & Lappegård, 2015; Régnier-Loilier & Vignoli, 2011; Toulemon & Testa, 2005). This is likely because they less often intend to have children in the short term and maybe less often have unrealistic time plans. When examining the models in which the desired time frame in which people want to have a child is not included (CHAPTER 3, Supplementary Material Table 4), we actually find that the higher educated have a child later, meaning that the reason why higher educated are not less succesful in realizing their fertility intentions is because they less often have short term plans.

With regard to labour force participation, it is argued that increasing female labour force participation is an important explanatory factor for the increasing age at first birth (Mills et al., 2011). However, this prediction may not be that straightforward: working more hours on the one hand results in greater financial resources to start a family but on the other hand results in work family conflict for women (Fahlén, 2013). A previous study from the Netherlands found that women with more working hours more often want their first child within three years, supporting the argument of the role of financial requirements (Begall & Mills, 2011). We found that men who work more expect to have children earlier but for women labour force participation did not influence their planned age to have their first child (CHAPTER 3, TABLE 2 and 3). Perhaps because the two contradicting mechanisms cancel each other out among women. Financial security, in the sense of having a permanent job was related to planning to have a child earlier for both men and women.

The models suggested that another practical consideration, people’s housing situation, was also important for family planning. Men and women who still live with their parents are planning to have a child later than those who rent or bought a house. Those who bought a house in turn make the transition to the first birth faster than those who are renting (CHAPTER 3, TABLE 2). These findings are in contrast to those observed in an Italian sample, where those who bought a house are less likely to make the transition to parenthood because buying a house and starting a family are both expensive and thus financially competing alternatives (Régnier-Loilier & Vignoli, 2011). However, the immediate costs of buying a house differ between countries (Mulder, 2006). For example, in the Netherlands people usually can get a mortgage of approximately the price of the house or a bit more while in Germany a down payment of 30% of the housing price is required. However, also in the Netherlands the height of the mortgage relative to the price of houses is decreasing, increasing also the direct costs for buying a house in the Netherlands. Therefore, the relationship between home ownership and family formation might also change in the Netherlands.

When it comes to normative factors, religion does not seem to play a role in this Dutch sample; those who are religious do not desire to have a child at a younger age and if anything, religious individuals slightly more often increase their desired age (CHAPTER 3, TABLE 2).
This is surprising because typically religious individuals are more likely to realize their fertility intentions (Philipov, Liefbroer, & Klobas, 2015). In our study in CHAPTER 3 we find that traditional gender roles do influence the desired timing to have a child, with those having more traditional values desiring to have a child sooner. A proposed reason why people plan to have children later is that people nowadays desire slightly smaller families (Sobotka & Beaujouan, 2014), which can lead to the feeling that they can afford to wait longer with their first birth (Mills et al., 2011). Our findings are in line with this latter expectation showing that men and women who expect to have more children also expect to have their first child at a younger age.

Unfortunately, in CHAPTER 3 we were not able to follow up individuals over their complete reproductive lifespan to see if those who expected to have a child later and continuously postponed childbearing were more likely to remain childless. However, we did show that those who planned to have a child later are least likely to actually have a child within the follow up period of 8 years (CHAPTER 3, Supplementary Material Figure 2). For men and women who are already a bit older and planned to have a child in a longer term, it is likely they will eventually remain childless.

From our findings in CHAPTER 3 we can conclude that a higher age at first birth is related to a sequence of decisions regarding the timing of having a child, and that every step in this sequence is influenced by both normative as well as practical considerations.

The need for fertility awareness

In CHAPTER 2 we find that many women remain childless despite the desire to have children in the future (and the same seems to hold for men, CHAPTER 2, additional information). In CHAPTER 3 we find that many men and women plan to have children at high ages. This raises the need for greater fertility awareness. A study in the UK and Denmark found that women who think that women are fertile up to higher ages desire to have a child at a high age themselves as well (Vassard, Lallemant, Nyboe Andersen, Macklon, & Schmidt, 2016). This indicates that women adjust their plans based on what they think is feasible. Even though many men and women are generally aware of decreasing fecundity with age, many underestimate the ability for women to have a child at specific ages, such as at age 30, 35 or 40 (Kudesia, Chernyak, & McAvey, 2017; Vassard et al., 2016). It is also likely that many men and women are not aware of the variability in the ability to have children up to certain ages (Harper et al., 2017). Due to this variability, some people can have children at a higher age while others are less capable to have a child at a higher age. These differences are caused by, amongst others, the biological factors that influence the ability to have children. For that reason, the following section will focus on these biological factors.
1.4 CHILDBEARING FROM A BIOMEDICAL AND
SOCIOMEDICAL PERSPECTIVE

Social science research on childlessness as well as on postponement of childbearing has
mainly focused on social factors influencing childlessness. However, in addition to the large
body of research that focuses on social factors, there is also a long biomedical research
tradition on childlessness and postponement of fertility. In this section I make a distinction
between the biomedical and genetic studies on childlessness.

1.4.1 Causes for infertility and subfertility

For women, ovulatory, cervical, fallopian tube and uterine problems are most likely to
cause infertility (Blundell, 2007). Two common diseases that are influential for remaining
childless among women are endometriosis and polycystic ovary syndrome. Endometriosis is
a disease that affects approximately 10% of premenopausal women and is characterized by
endometrial-like tissue outside of the uterus causing pelvic pain and subfertility (Nnoaham
et al., 2011). The risk of infertility is about 20 times greater for women with endometriosis
(Strathy, Molgaard, Coulam, & Melton, 1982) and 25-50% of women with infertility have
endometriosis, with 30-50% of women with endometriosis experiencing infertility. Polycystic
ovary syndrome (PCOS) is characterized by chronic oligo- or anovulation, hyperandrogenism
(biochemical and/or clinical evidence of male hormone excess) and polycystic ovarian
morphology (Ehrmann, 2005). About 5-15% of women in reproductive ages have PCOS
(Balen et al., 2016), and this accounts for 80% of the anovulatory infertility.

For men, sperm defects are the most likely cause for infertility (Blundell, 2007).
Azoospermia, which is a zero sperm count, effects around 1% of the male population, and
is the reason for infertility in 10-15% of men (Willott, 1982). Also oligozoospermia, which is
a sperm count of less than 15 or sometimes 20 million per milliliter in the semen (Cooper et
al., 2010) is related to difficulties in having children.

1.4.2 Postponement of childbearing from a biomedical perspective

Linking this biomedical research to postponement of childbearing, it should be noted that
there is substantial variation in the extent to which people are able to have children at
higher ages. Firstly by looking at age at last childbirth in natural fertility populations, it
appears that there is large variation in the age up to which women can give birth to a child
(Eijkmans et al., 2014). Some women, although likely very few, are not able to have children
around age 25, while other women are still able to have a child at age 45. Reasons for these
differences in declining fecundity with age are, amongst others, differences in depletion of
ovarian follicles, differences in regularity of ovulatory cycles or differences in hormone levels
(Towner, Nenko, & Walton, 2016). Information on for example age at menopause further
shows that on average women go through menopause around age 50, but there is a lot of
variation around this age, with some women already having their menopause at age 40 and
others at age 60 (te Velde & Pearson, 2002). Given that already 10 years prior to menopause
the ability to have children strongly decreases, this shows that there is a large variation in
female fecundity by age (te Velde & Pearson, 2002). Thus, for some women postponement of childbearing attempts up to higher ages will not result in remaining childless, while other women who wait until the age of 30 or 35 will experience difficulties in getting pregnant and might remain childless.

1.4.3 Genetic influences on reproductive traits
Genetic studies generally focus on the way in which genes cause variation in an outcome of interest. An important concept in genetic research is heritability, which is the extent to which variation in an outcome can be attributed to genetic variation. This is often examined using the classical twin method (See Box 2 for information on different methods that are used to assess how genes influence behavior).

Genetic studies convincingly show that many traits that are related to remaining childless are heritable. For example, twin studies found that the time frame in which women can have children is partly heritable, with heritability of around 50% for age at menarche (i.e., first menstruation) and a genetic component of around 60% for age at menopause (i.e., last menstruation) (Snieder, Macgregor, & Spector, 1998). Also diseases that can cause difficulties with having children are heritable; for endometriosis twin studies show a heritable component of around 52% (Treloar, O’Connor, O’Connor, & Martin, 1999) and for PCOS heritability is estimated at around 72% (Jones & Goodarzi, 2016).

Recent developments in the field of (behavior) genetics steered away from heritability studies, and instead started to focus on finding specific genetic variants related to a trait (see Box 2 for an explanation of the methods used). A method commonly used is the genome wide association study (GWAS), which assesses associations between genetic variants and a trait of interest. Specific genetic variants have already been found to be related to PCOS (Hayes et al., 2015), endometriosis (Painter et al., 2011), age at menarche (Day et al., 2017) age at menopause (Day et al., 2015) and sperm defects (Aston & Carrell, 2009).

1.4.4 Genetic influences on reproductive behavior
Over the last decades, a new field of research developed that focused on the genetic influences of fertility outcomes. With fertility outcomes I mean actual observed fertility behavior of individuals, such as whether they have a child at the end of their reproductive period or the age at which they have their first child (as opposed to genetic research that focuses on factors that influence fecundity such as endometriosis and age at menopause). As reviewed by Mills and Tropf (2015), twin studies showed that the heritability of the number of children ever born (NEB) to a person is around 40% and heritability is estimated to be around 25% for the age at which people have their first birth (AFB). Genetic effects have also been detected for the age at which people first try to have a child (which can be seen as an indicator of fertility desires) using twin studies (Rodgers, Kohler, et al., 2001). These approaches have recently been extended by a GWAS study on fertility outcomes, which isolated genetic markers related to AFB and NEB (Barban et al., 2016).
Box 2  Methods in genetic research

The twin method
The oldest method which is used to estimate heritability (the extent to which variation in an outcome can be attributed to genetic variation) is the classical twin method. This twin method is based on the principle that monozygotic (MZ) twins share all of their genes, while dizygotic (DZ) twins share only 50% of their segregating genes. MZ and DZ twins share their environment to the same extent, and therefore greater similarity in a trait among MZ twins should be due to their greater genetic similarity (Boomsma, Busjahn, & Peltonen, 2002). Put very simply, when the similarity (correlation) between MZ twins is greater than the similarity in DZ twin pairs, twice the difference in this correlation is the heritability. For example, when the correlation of age at first birth is 40% in MZ twins and 24% in DZ twins (as in the paper by Tropf et al. 2015), this difference is 16% (which is due to the 50% greater genetic similarity among MZ twins) and twice this difference (to account for 100% of the genetic variation) is 32%, thus an estimated heritability of 32%.

Molecular genetic methods
More recently, molecular genetic data has been used to examine the influences of genes on behavior or diseases. Basically, the largest part of the DNA sequence is the same in all humans. However, on a small part of the DNA, mutations occur, which result in genetic variation. This genetic variation makes us different (Fagerness & Nyholt, 2008). The most abundant type of genetic variation is the single nucleotide polymorphism (SNP), which is the variation of a single nucleotide that occurs at a specific position in the genome. On every SNP, an individual can have either 0, 1 or 2 risk alleles. Risk alleles are the genetic variants that increase the chance of the outcome of interest. Genotyping is the process in which information on genetic variants (specifically SNPs) in individuals is measured. More and more large datasets, both datasets collected for medical research as well as social science research, include genotyped information of their respondents, allowing researchers to use this information to examine the influence of genes on diseases or behavior.

GWAS
Genome Wide Association Studies (GWAS) test for associations between SNPs and a trait of interest (McCarthy et al., 2008). For example, for age at first birth, for every SNP it is examined if people with no risk alleles differ in their age at first birth from people with one or two risk alleles. Because many SNPs are measured—recent genotyping platforms measure approximately 1 million SNPs—the number of false associations you are expected to find is large. For this reason, these associations are tested with very stringent p-values of 5x10-8.
Chapter 1

Box 2   Methods in genetic research

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Synthesis

GREML method

Genotyped information can be used to find specific genetic variants related to a trait of interest, as is done in the GWAS method, but it can also be used to estimate heritability. Estimating heritability with genotyped information is done with the genomic-relatedness-matrix restricted maximum likelihood (GREML), which simultaneously considers the additive effect of all genotyped SNPs (Yang et al., 2010). This method is based on the same principle as the twin method; if people who are genetically more similar are also more similar in a trait of interest, this indicates that the trait is heritable. The difference between the twin and GREML method is that the GREML method uses information on unrelated individuals. This GREML method contains two steps. First, for each pair of unrelated individuals, the genetic similarity is estimated based on similarity in SNPs. Second, this genetic relatedness is used to explain similarity in an outcome. This is done by a comparison of a matrix of pairwise genomic similarity to a matrix of pairwise phenotypic similarity.

Twins in GREML method

This GREML method can also be used to improve estimates from the classical twin method. The classical twin method assumes that all DZ twins share 50% of their segregating genes. However, just like regular siblings, DZ twins share between 35% and 65% of their segregating genes (Visscher et al., 2006). For this reason, the twins in GREML method uses more precise information of genetic similarity than the classical twin method.

Genetic risk scores

Information from GWAS studies can be used to create genetic risk scores. A specific type of genetic risk score is the polygenic risk score (PGS), which is the sum of the risk alleles weighted by their effect size and is thus a summary measure of genetic variants that increase the risk for a trait (Wray et al., 2014). Different risk scores can be created depending on the selection of SNPs included in a risk score. This ranges from using only genome wide significant SNPs (p-value of 5x10^{-8}) to including all genotyped SNPs (p-value of 1).
Previous genetic studies mainly focused on AFB and NEB. None of the previous studies focused specifically on childlessness. Examining genetics of childlessness is possibly particularly illuminating, because the biomedical underpinnings of infertility may well have a genetic component.

1.4.5 The heritability of childlessness
In CHAPTER 4, we therefore examine whether there is a genetic component to childlessness. We use data from the Swedish Twin Registry on men and women, which allowed us not only to examine heritability, but also to examine sex differences in heritability. First of all, using the classical twin method (see Box 2) we found heritability estimates around 50% (CHAPTER 4, FIGURE 2). This estimate is even higher than the heritability estimates for the total number of children that people have (which is estimated to be around 40%, Mills and Tropf 2015). We expand these findings by using the genetic data from the twins in with the GREML method (see Box 2). This method uses more precise information on genetic similarity, and thus can give a more precise estimate of the extent to which genes can explain variation in a trait. With this method we find even higher estimates of heritability: 59% in women and 56% in men.

A risk of the twin method as well as of the twins in GREML method is that it uses information on related individuals and therefore estimates could be biased upwards due to shared environmental influences. To overcome this limitation, we expanded these findings by using polygenic risk scores for unrelated individuals (PGSs, see Box 2 for an explanation of this method) of genes related to AFB. Also with this method—for which we only use one twin of each twin pair, and thus only include unrelated individuals—we find that genes influence childlessness.

1.4.6 Predictive power of genetic risk scores compared to social factors
In our twin study (CHAPTER 4) we found that the heritability of childlessness is about 50%. However, results from twin studies cannot be used to examine individual risks for remaining childless, because twin studies provide estimates of the amount of variation due to genetic variation, but they do not provide information on individual genetic risks to remain childless. For that reason, in CHAPTER 5 we include both PGSs (see Box 2 for an explanation) as important predictors of childlessness. This is likely due to the GWASs with small sample size on reproductive behavior explain less than 1% of the variance. What is noteworthy is that the PGSs for reproductive behavior explain less than 1% of the variance in reproductive behavior. This is surprising because we know that these traits are strongly associated with reproductive behavior. For example, genes that would influence your fertility desires or that would result in an early age of menopause would not result in childlessness in time periods in which there were strong societal norms to have children and to have them at young ages. Secondly, non-additive genetic effects or new genetic mutations might restore genetic variance lost to selection. A third possible reason might be that different genes play a role in childlessness among men and women, and therefore genes that increase the chance of childlessness among men can be passed on through female lineage and vice versa (Hughes & Burleson, 2000).
well as socio-environmental factors in a model to explain childlessness. With this approach we can answer the question the extent to which genetic risk, in comparison to well-known social factors, can explain whether an individual remains childless.

We observed that genetic risk scores can only explain a very small part of the variation in remaining childless. PGSs for the fertility outcomes (AFB and NEB) have some predictive power in explaining why people remain childless; genes associated with a later AFB and lower NEB are positively related to remaining childless (CHAPTER 5, TABLE 1-4). The effects, however, are small; all PGSs combined explain less than 1% of the variance in reproductive outcomes, whereas social factors, including birth year, educational attainment, age at marriage, first occupation and religion, can explain between 20 and 48% of the variance (CHAPTER 5, TABLE 1-4).

PGSs for biomedical outcomes, such as endometriosis or PCOS, do not predict whether someone will become a parent or not. This is surprising because we know that these traits are strong predictors of childlessness. This is likely due to the GWASs with small sample size on which these PGSs are based. As can be seen in TABLE SA2 of CHAPTER 5 the sample sizes of the GWASs for male biomedical outcomes are all under 1.000 individuals, and the GWAS for PCOS and endometriosis only approximately 4.000 and 10.000 individuals respectively (for comparison, the GWAS for NEB includes 340.000 individuals). The reason why sample size is important is that GWA studies test hundreds of thousands of independent effects with very stringent p-values, and thus very large sample sizes are required to achieve sufficient power to detect true effects (Hong & Park, 2012).

1.4.7 High heritability estimates, low predictive power of polygenic risk scores
What is noteworthy is that the PGSs for reproductive behavior explain less than 1% of the variation in childlessness, whereas in our twin study in CHAPTER 4 we find a heritability of almost 50%. The discrepancy between heritability and predictive power of PGSs has been observed for many other traits (Nolte et al., 2017). This phenomena of much larger heritability estimates from twin studies compared to SNP based studies such as GWAS and PGSs has been called missing heritability (Manolio et al., 2009).

There are several suggested reasons for the discrepancy between findings from twin studies versus PGSs. A first explanation might be heterogeneity across the discovery samples (Tropf et al., 2017), because GWAS studies (where the PGSs are based on) often include individuals from many different countries to obtain large samples. This means that only genetic variants that are related to a trait of interest uniformly across all populations are being picked up. This is likely very relevant for a trait like childlessness, as the study by Tropf and colleagues (2017) showed that there is a much smaller proportion of SNPs that is uniformly related to age at first birth and number of children born, then for example related to height. Another explanation might be that twin studies also pick up non-additive genetic effects such as dominance and epistasis, while GWASs only capture additive genetic effects. However, several studies reject this idea and do not find strong dominance effects (Nolte et al., 2017; Zaitlen et al., 2013). Furthermore, GWASs only include common genetic variants, while it is estimated that rare genetic variants also explain a substantial part of the heritability of many
outcomes (Visscher, Yang, & Goddard, 2010). This might especially be the case for infertility, as for example with regard to male factor infertility it is suggested that rare genetic variants are important (Hotaling & Carrell, 2014).

Another explanation is that estimates from twin studies are actually overestimations, due to a violation of the equal environment assumption (Felson, 2014). The equal environment assumption implies that monozygotic and dizygotic twins share their environment to the same extent, and therefore differences in phenotypic similarity are due to differences in genetic similarity and not differences in their shared environment. A study that extensively examined this assumption by assessing extent to which environmental similarity (contact and intimacy between twins, shared friends etcetera) explained heritability estimates, found that MZ twins share their environment more than DZ twins do, especially during childhood. However, when controlling for this similarity, heritability estimates barely decrease, and therefore it was concluded that the heritability estimates would not be substantially overestimated due to a violation of the equal environment assumption (Felson, 2014).

Something to keep in mind when evaluating the explained variance from genetic risk scores, is that in the social sciences in general, the explained variance from only one predictor is never really high, and the low explained variance from the genetic risk scores should be seen in this light. For example, when looking at explained variance of childlessness by education (one of the most important factors in childlessness), in the Health and Retirement Survey, the explained variance is only 2.5%. In comparison to 2.5%, the explained variance by the genetic risk scores is not that much lower.

There is reason to be optimistic about the future predictive power of GWASs and PGSs. As larger GWASs are being conducted, more and more SNPs are found to be related to outcomes. For example, with regard to educational attainment, in 2003 a GWAS was conducted among 101,069 individuals, in which three significant SNPs were found (Rietveld et al., 2013). In 2006, 74 genome wide SNPs were identified when the sample size was expanded to 293,723 individuals (Okbay et al., 2016). In 2018, with a sample size of over a million individuals (N= 1,131,881) 1,271 SNPs were discovered in relation to educational attainment (J. J. Lee, Wedow, & Okbay, 2018). The increase in the number of significant SNPs that are associated with an outcome also increase the predictive power of genetic risk scores, with 2.5 to 4% explained variance from the genetic risk scores from the 2013 GWAS, 6 to 7% explained variance from the 2016 GWAS and 11 to 13% from the most recent GWAS for educational attainment. Also currently a larger GWAS is being conducted on AFB and NEB (Mills et al, forthcoming). In the previous GWAS on AFB and NEB, which we used to create the PGSs in CHAPTER 5 of this dissertation, explained variance for NEB was 0.2% and for AFB was 0.9% (with sample sizes of 343,072 for NEB and 251,151 for AFB) (Barban et al., 2016). In the new GWAS, sample sizes approximately doubled to 717,062 individuals for NEB and 542,901 for AFB and with this the predictive power also doubled to 0.5% for NEB and 1.8% for AFB. The finding that greater GWASs result in greater predictive power of PGSs is also found in a study that assesses the predictive ability of PGSs for 32 complex traits, in which the PGS for the trait for which most significant SNPs were found, namely 635 SNPs for human height, is most predictive, with an explained variance of 15% (Nolte et al., 2017).
1.4.8 Sex differences in the genetic influence on childlessness

One of the reasons why it is suggested in the literature that heritability of childlessness is not as counterintuitive as it sounds (see footnote 4), is that different genes might influence male and female fertility (Hughes & Burleson, 2000). For this reason, we examined the extent to which different genes influence childlessness among men and women. This can be investigated by looking at the genetic correlation between childlessness in men and childlessness in women. A genetic correlation of 1 between men and women would imply that the same genes influence childlessness in men and women, a genetic correlation of 0 would indicate that different genes influence men and women, while a genetic correlation of -1 would imply that the genes that increase the probability to remain childless in men would decrease the probability to remain childless in women (and vice versa). We find in CHAPTER 4 that different genes play a role in childlessness for men and women. By comparing similarity in childlessness between same sex and opposite sex twin pairs in a twin model, we find a genetic correlation that is not significantly different from 0, indicating that different genes are involved in childlessness for men and women. Via the GREML method we find a small negative estimate of -0.2, suggesting that genes that increase the probability of remaining childless in women decrease the probability of remaining childless in men. Also when using a different approach, namely assessing the influence of PGSs for age at first birth and number of children born on childlessness, we find in the Swedish sample (CHAPTER 4) as well as in two samples in the US (CHAPTER 5) that these genetic risks are weaker in male compared to female samples and are insignificant in the male sample. In the Swedish sample we find that the genetic risk scores for AFB increase the chance of remaining childless among women but not among men. In the two US samples we find the same; AFB genetic risk scores increase the chance of remaining childless among women but not among men. The genetic risk scores for NEB have a weak negative effect on both men and women in the two US samples, and no effect in the Swedish sample.

This hints towards the idea that some genes that increase the chance to remain childless in women might not influence the chance of becoming a parent in men. An explanation for this finding could be that both the biological and the social pathways leading to childlessness are different for men and women, and these pathways can be influenced by genetic factors. For example, educational attainment is positively associated with childlessness in women but less so in men (Keizer et al., 2008). Given that education is partly heritable (Branigan, McCallum, & Freese, 2013), it might be the case that those genes related to education also have a positive influence on childlessness among women, but no effect or even a negative effect on men. Also, for example, testosterone levels increase fertility in men but decrease fertility in women (Barbieri, 2000). Testosterone levels are heritable (Sloyter et al., 2000) and thus genes related to testosterone levels might decrease the chance of childlessness among men but increase this chance among women.

1.4.9 Genetic risk and postponement of childbearing

Although previously studied in isolation, it is reasonable to assume that genes and environment do not influence childlessness in a simple additive way. On the one hand we
know that genes play a role in traits that influence a decline in fecundity at a certain age, such as an early age at menopause. On the other hand we know that the environment can cause individuals to postpone attempts to have children (Castles 2003; Thévenon 2009, CHAPTER 3). This postponement of childbearing is likely to result in childlessness (CHAPTER 2). However, there are large differences in the age at which people experience difficulties with getting pregnant, and these difficulties might be partly genetically explained. At younger ages many people are probably able to have children, but at higher ages there is much more variation; it may thus be that particular genetic effects are much stronger in later life than in early life.

In CHAPTER 5 we, therefore, examine the interaction between the age at which people get married (as a proxy for the age at first attempt to have a child) and genetic risk scores. We found some suggestive evidence that genes that are associated with a higher age at first birth are especially relevant for remaining childless among women who get married at higher ages (CHAPTER 5, Figure 2). We found this only among women, for whom we know the biological abilities to have children decreases with age more steeply than for men. This could indicate that biological abilities become more important at higher ages. There could however be another explanation for the interaction between the genetic risk score for AFB and age at first marriage. The genetic risk score for AFB could of course capture the biological abilities to have children, but it could also be an indicator of fertility desires, as previous studies found that fertility desires are partly heritable (Kohler, Rodgers, & Christensen, 1999; Miller, Bard, Pasta, & Rodgers, 2010) and that people who desire fewer children attempt to have children at higher ages (Miller, Bard, et al., 2010). In this case the interaction would indicate that those people who get married at higher ages and have lower fertility desires will not have children, while those who get married at higher ages and have high fertility desires will still have children. A reason why genes related to fertility desires would be less influential among men and women that get married at younger ages could for example be that men and women who get married at younger ages are from more traditional backgrounds (McLaughlin, Lichter, & Johnston, 1993), where the norms to have children are stronger and thus individual desires less influential. The PGSs for the biomedical traits (age at menopause, endometriosis etcetera) showed no interactions with age at first marriage. However, this is possibly explained by the low predictive power of these risk scores.

1.4.10 Genetic risks across cohorts
Several studies suggest that genetic effects may differ across time periods and across countries. In the US (Briley et al., 2015), the UK (Tropf et al., 2015) and Denmark (Kohler et al., 2002) findings from twin studies indicate that heritability of reproductive-related outcomes was higher around the second demographic transition, for individuals born between 1935 and 1950, than in periods before and after. The period in which those individuals born between 1935 and 1950 were of childbearing age, namely around the 1970s, is seen as a period in which norms were changing and thus individuals had great freedom in their behavioral choices. Using an entirely different approach, Tropf and colleagues (2017) also found evidence for the idea that genetic influences are context and birth cohort specific. In this study genetic similarity...
among unrelated individuals was used to demonstrate that within country and birth cohort genetic similarity is more strongly related to similarity in fertility outcomes than across countries and birth cohort. In other words, there are differences in the relationship between genes and reproductive outcomes over time and place.

The reason why genetic effects differ across birth cohort could be due to different societal norms regarding fertility behavior. For example, in time periods or countries in which childbearing is postponed up to higher ages, it is likely that genetic factors related to decreasing fecundity, such as early menopause, are more influential in remaining childless. Alternatively, in time periods in which there is a strong societal norm to have children, the main reason why couples remain childless are biomedical reasons, and these biomedical reasons might be heritable. In contrast it is argued that genetic propensities and thus heritability of fertility outcomes should be higher where individual freedom is more pervasive, due to the rise in realization of individual genetic drivers for example related to fertility desires (Kohler, Billari, & Ortega, 2002).

To further test the idea that genetic influences on fertility differ by birth cohort, we took yet another approach in CHAPTER 5 where we assessed the extent to which PGSs for AFB and NEB have a different influence on childlessness in different birth cohorts. We did not find that genetic risk scores have a different effect on remaining childless depending on birth cohort. This could be because finding a gene-environment interaction using GWAS information is difficult because the genes that are found in the GWAS are the ones that are pervasive, due to the rise in realization of individual genetic drivers for example related to fertility desires (Conley, 2017).

1.4.11 Overlapping genetic and environmental influences

Many twin studies as well as a recent GWAS showed that genetic variations explain AFB and NEB (Barban et al., 2016; Mills & Tropf, 2015), and in CHAPTER 4 we show that also childlessness is partly explained by genetic variation. It is however not straightforward how genetic variations result in remaining childless. When the specific SNPs that were found in the GWAS for AFB and NEB were examined, some of them were related to biomedical factors for fecundity, such as endometriosis and sperm defects, while some of these SNPs were also associated to cognitive function (Barban et al., 2016). Therefore, the effect of these genetic risk scores on childlessness could be through their effect on education (as a potential outcome of cognitive function), which is typically associated with a higher likelihood of childlessness (see Chapters 2, 3 and 5) or through their effect on biomedical factors (sperm defects or endometriosis). Another pathway might be through the genetic influences on fertility desires (Rodgers, Kohler, et al., 2001).

Attempts to ascertain through which pathways genes influences fertility, have been made in previous research. A twin study from the UK and the US found that about 40% of the genetic influence on NEB is shared with genetic influences on age at marriage and AFB (Briley et al., 2017). The genetic effects of AFB in turn are largely explained by genetic effects of age at first marriage (Briley et al., 2017). There is also a shared genetic basis
between education and fertility (Barban et al., 2016), suggesting that the causal effect of education on fertility is mainly due to shared genetic influences (Nisén et al., 2013; Tropf & Mandemakers, 2017), although also shared environmental influences partly explain the relationship between education and fertility (Tropf & Mandemakers, 2017).

In CHAPTER 5, we contribute to the research that attempts to scrutinize the pathways through which genes influence fertility by examining the relationship between the genetic risk scores of AFB and NEB with education, religion, age at first marriage as well as the relation of the genetic risk scores of AFB and NEB with the genetic risk scores for medical factors related to childbearing (PCOS, endometriosis etcetera). We found that the effect of the AFB and NEB risk scores is correlated to education and age at marriage, and that these latter factors mediate the relationship between the genetic risk scores and childlessness, reducing the effects for about 50% (see CHAPTER 5 Table 6 and Table 7). Our findings are thus in line with findings from previous research conducted in twin samples, that a part of the genetic influence on fertility outcomes is through genetic effects on education and marriage.

We also had a look at the overlap between the genetic risk scores for AFB and NEB with genetic risks associated with the biological reproductive traits. This could show the extent to which the genetic factors influence childbearing through biomedical pathways. For women we found a positive correlation between genetic risks associated with a later age at menarche, later age at first birth and later age at menopause (see CHAPTER 5 Table 6). This could be interpreted as one set of genes that delay biological maturation and development, resulting in an overall biological shift to fertility in later life (Mostafavi, Berisa, Przeworski, & Pickrell, 2016). Given that the genetic risk for a greater age at first birth is positively related to childlessness, it could be the case that this delay in biological maturation could result in remaining childless. When we examine the extent to which the PGSs for age at menarche and menopause mediate the effect of the AFB PGS, we find that this is negligible. We did not find clear associations between the genetic risk score for AFB and NEB with PCOS and endometriosis. For men, we observed no associations between the genetic risks for AFB and NEB with the genetic risk for the biological reproductive traits. These small and null-findings could be due to the low predictive power of the genetic risk scores for these biological reproductive traits.

In conclusion, we found that genetic factors play a role in remaining childless. Our findings that genetic factors are more important among women who postpone childbearing, as well as the findings that genetic factors overlap with the age at marriage and educational level, stress the importance of an sociogenomic approach in which simultaneously the role of genetic and socio-environmental factors is assessed.

1.5 DIRECTIONS FOR FUTURE RESEARCH

1.5.1 Research on the consequences of different pathways to childlessness

From our research we find that many people are remaining childless despite the desire to have children for a large part of their life. Previous research that examined consequences
of childlessness often simply made a distinction between consequences of voluntary and involuntary childlessness. Future research should pay more attention to how different pathways to childlessness result in different consequences. One study that examined how different reasons for childlessness related to different outcomes shows that women who are childless due to biomedical reasons were most affected by not having children; they most often feel sad when they see pregnant people or when they compare themselves with people with children (McQuillan et al., 2012). However, also women who remain childless due to situational barriers such as not being financially ready or having a right partner, as well as women who gave no specific reason for being childless, more often experience childlessness concerns than women who are voluntary childless. This stresses the importance of not making a simple distinction between women who are not able to have children, and women who are voluntary childless, because under this simple dichotomy, those with situational barriers or without specific reasons would be considered voluntary childless, even though they likely do not experience their childlessness as voluntary. More research should focus on which pathways women took that resulted in remaining childless, and how this translates into childlessness concerns and well-being.

1.5.2 Studies on the contextual influences on unintended childlessness

A proposition from our study on the translation from desiring to have children into remaining childless is that many women remain childless due to the difficulty in combining family life with working (CHAPTER 3). However, the country in which a woman lives affects how difficult the combination of work and family is. Previous research strongly suggest that for women the extent to which combining a full-time job with having a family is dependent on whether there is childcare available and the extent to which men are involved in childrearing and housework (Baizan, Arpino, & Delclòs, 2016; Harknett et al., 2014; McDonald, 2000a). These previous studies often focused only on the number of children that people have and not the combination of fertility preferences with outcomes.

A study that examined the extent to which the gap between the intention to remain childless and actually remaining childless is context specific found that in all of the 20 European countries studied as well as in the US many more women remain childless than intend to remain childless, and that this gap is greatest among the higher educated women in almost all of the countries in which this was studied (Beaujouan & Berghammer, 2017). However, the size of this gap differs greatly between countries, and also the extent to which this gap differs between the educational groups varies between countries. Future research could examine what factors cause the gap between the desire to remain childless and actually remaining childless across different contexts, both at the individual and on the societal level. This type of research should improve understanding on how in different contexts men and women experience constraints in realizing their fertility intentions and the extent to which this causes unintended childlessness.
1.5.3 Research on contextual factors for childlessness versus number of children

Many previous studies focused on family policies and how they influence the number of children people have. Findings show that family policy has a stronger impact on second and third births than on first births (Harknett et al., 2014). In line with these findings on stronger policy effects on number of children than on childlessness is research that finds that the educational gradient to number of children (higher educated women have fewer children) is decreasing or even reversing in Nordic countries, which are characterized as countries that actively support the compatibility between work and family life. Yet, the educational gradient in childlessness still exists here (Neyer & Hoem, 2008; Wood, Neels, & Kil, 2014).

A suggested reason is that women care more about practical considerations for second and third births than for first births. Before the birth of the first child people are likely not fully aware of the amount of work a child involves, and are not yet aware of the consequences of the presence or absence of child-support policies. Studies on another proposed solution for unrealized fertility, namely greater involvement of men in the household, suggests that the effect of equal division of housework seems to be mainly influential on higher order births than on first births (Mills, Mencarini, Tanturri, & Begall, 2008; Torr & Short, 2004). This is possibly because once a first child is born there is much more work to be divided, and that once a first child is born the division of household work often becomes much more unequal. Further research should investigate why women are less responsive to family policies when it comes to having a first child than to subsequent childbirths, and how policies should be efficient in decreasing the gap between the desires to have a child and actually having a child.

1.5.4 Men need to be studied

In our studies, as well as in previous research, we find that social factors influence men and women differently. Education does not or negatively influences childlessness in men while it increases the chance of remaining without children in women, and different genetic risks seem to be influential in men and women. Not many previous studies examined men, and especially research with regard to fertility intentions in men is scarce. The findings from Chapter 2, supplements however seem to suggest that men who are higher educated and working more hours less often desire to remain childless. Also, previous research found that many men, just as women, remain childless despite the desire to have a child in the future (Kessler et al. 2013, Chapter 2, supplements). A few studies examined the relationship between gender norms and fertility desires among men, but results are mixed (Goldscheider, Oláh, & Puur, 2010; Puur, Olah, Tazi-Preve, & Dorbritz, 2008; Westoff & Higgins, 2009). Some previous studies suggested that men who are living in societies where more is expected from men in terms of parental involvement, some men, and especially career oriented men might steer away from parenthood (A. Jensen, 2010). This is interesting since greater involvement of fathers in childrearing seems to be on the agenda in Europe, as the European commission just voted in favor of an expansion of paternity leave. The new regulations prescribe that all parents get 10 days of leave after the birth of a child and have the right of six weeks of paid parental leave (Spekschoor, 2018). In Sweden father’s parental leave was already extended since 1974 but the increase in uptake of leave happened very slowly (Duvander
& Andersson, 2006). More research should examine what factors influence fertility desires of men and how and when these desires are translated into outcomes. It would also be interesting to examine how greater expected involvement of men in childrearing changes their actual parental involvement and fertility desires.

1.5.5 A couples’ perspective on childlessness
Although some individuals are remaining childless because they did not have a partner during their reproductive life span, some are remaining childless while being in a relationship. Gains can be made from examining childlessness from a couples’ perspective. There are some findings that especially deserve attention on the couple level. The first is the contradictory finding that higher educated women more often remain childless and higher educated men less often remain childless, while we also know that there is educational assortative mating; which is that higher educated men tend to marry higher educated women and vice versa (Mare, 1990). Also findings regarding gender equity deserve attention on the couple level, as greater gender equity predicts higher fertility for women and lower fertility for men, while at the same time at the couple level gender equity in terms of the division of household tasks should be the same. Studying couples could shed light on these counterintuitive findings. Another venue of further research could be regarding genetic assortative mating, as previous studies found that people tend to marry individuals who are genetically similar to themselves. For example, genetic assortative mating occurs with regard to height, BMI and educational attainment (Conley, Laidley, Belsky, Fletcher, & Boardman, 2016; Conley, Laidley, Boardman, & Domingue, 2016; Domingue, Fletcher, Conley, & Boardman, 2014; Guo, Wang, Liu, & Randall, 2014; M. R. Robinson et al., 2017). Combining these findings with our findings on genetic influences on fertility, it would be interesting to examine whether there is genetic assortative mating regarding fertility desires and how this influences whether couples remain childless. Also using information of genetic risks of both partners would probably increase predictive power.

1.5.6 The future of genetic research on fertility
In this dissertation we found that genetic factors are important for remaining childless, with research using whole-genome data showing that we can eventually expect that the upper level estimates of the genetic ‘SNP-heritability’ of fertility (number of children ever born, age at first birth), will range from 10-15% respectively (Tropf, Stulp, et al., 2015). With current sample sizes and techniques, the predictive power of PGSs remains lower than some of the social science variables. This is logical since we would only expect genetic effects to be partially responsible for an outcome such as childlessness, which is not only genetically, but also largely socially determined. It is vital to note that as researchers we never simply examine the direct effect of one variable in a multivariate model, which also holds for genetic variables. The findings of the predictive power of PGS for example with regard to human height and educational attainment show that as samples to discover genetic risks increase, predictive power of PGSs increase. More recently, the PGS for educational attainment ranged from 10-11% of the entire predicted variance (J. J. Lee et al., 2018), lower but still quite

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similar to the classic social science predictors of parent’s education. A forthcoming extension of the GWAS reproductive behavior study (Barban et al., 2016) also expands from 12 to around 400 loci for many fertility variables, with a higher predictive power of around 4-7%. Put in perspective, the direct effects of classic social science predictors of childlessness and fertility outcomes when entered alone in a model explain around 6 – 15% of the entire variance (Mills, Barban, & Tropf, 2018). Particularly since the GWAS studies examine the biological functions of genetic loci, for childlessness, or low fertility in general this could possibly in the future result in the possibility to inform individuals about their individual risks for infertility at certain ages. This would be useful because many men and women are not aware of the variability in the ability to have children up to certain ages (Harper et al., 2017) and are of course not aware of their own age up to which they are less likely to have children. Our findings seem to be suggesting that genetic risks are especially important for women who start childbearing attempts at higher ages. When predictive power of PGSs increases, the relationship between genetic risks and age should be examined further.

The possibility of using personalized genetic risk has been widely discounted and should be considered with caution. On the one hand informing people about their genetic risk could be a positive development; men and women in their twenties might want to be informed about the question of “how late they can wait”. Those who are aware of their own genetic predisposition to, for example, early menopause might behave accordingly. They might start their childbearing at earlier ages which might increase their chances of having a child. Alternatively, they might already at earlier ages consider other options to become a parent, such as adoption. On the other side there might also be risks related to personal genetic predictions. While social factors influencing fertility are often considered to be probabilistic, they increase or decrease the chance to remain childless but these effects are not absolute, genetic effects are often perceived to be deterministic. Genetic influences on childlessness may be perceived as translating directly into childlessness. Some research that focused on people that examined their personal genetic risk showed that people seemed to be interpreting their results with nuance (Saukko, 2013). Another reason for caution might be with regard to the marriage market. Nowadays when couples find out they are not able to have children, they are often together already for a while and might not split up solely because one of the partners is not able to have children. When personalized genetic risks would be very advanced, partners might consider those not able to have children as unsuitable partners. So although there might be advantages to being able to make personal genetic predictions, we have to be aware of the risks of undesired consequences.
1.6 CONCLUSIONS

1.6.1 Childlessness is often unintended
This synthesis started with the notion that childlessness in many Western countries is high in present times, while at the same time the desire to remain childless is not at all common. Indeed, childlessness if often unintentional or undesired. Given that childlessness is not mainly driven by individual desires, and thus likely often unplanned, the aim of this dissertation was to examine what causes childlessness.

From our first study we confirm the idea that childlessness is often unplanned, since many women who eventually remain childless, intended to have a child for a large part of their life. Also our second study on desired fertility timing shows that many men and women who intend to have children, want them at high ages which is likely to translate into childlessness. Of course, although childlessness was not planned, it could still be desired later in life. Previous studies suggested that women who postpone childbearing up to higher ages might get used to their childfree life and enjoy the freedom and leisure time (Buhr & Huinink, 2017).

1.6.2 Genetic influences are important and related to social factors in explaining childlessness
Drawing further on the notion that childlessness is likely often undesired, the genetic factors related to childlessness were considered. Firstly, we find that childlessness is to a large extent heritable. However, from this observation we cannot draw straightforward conclusions about the extent to which childlessness desired and due to biological factors, because the genetic influence on remaining childless does not only capture the biological abilities but could also capture genetic influences on fertility desires. When taking a different approach, and assess how genetic risk scores influence childlessness, we again find that they influence childlessness and that this is partly through the effect of education and marriage on childlessness, which stresses the importance of studying genetic and social factors simultaneously. We also have to conclude that the predictive power of genetic risk scores at this point remains lower than for social science variables but as sample sizes of GWAS studies are getting bigger the predictive power of genetic risk scores will also increase.
Can fertility desires and expectations explain the association of education and occupation with childlessness?

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