

Unravelling gene-environment interaction and fertility

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Introduction: Research problem and previous research

There has been a massive delay in the age at first birth across Europe since 1970, which is now between 28-29 years (Mills et al. 2011). A primary reason for fertility postponement is the clash between the optimal biological period for women to have children with obtaining a higher education and building a career (Rindfuss et al. 1996; Brewster & Rindfuss 2000; Mills et al. 2011). The ability to control childbirth through contraceptives and cultural transformations surrounding the role of children has also played a central role (van de Kaa 1987). Explanations for changes in fertility behaviour in demography and sociology have almost exclusively relied on socio-environmental factors (Brewster & Rindfuss 2000; Kohler et al. 2002; Kravdal & Rindfuss 2008; Goldstein et al. 2009; Hobcraft, 2007).

The role of genetic endowment and their interaction with the environment (gene-environment interaction (GxE)), has been scarcely investigated. However, an increasing body of literature indicates an interplay between genetics, environment and fertility. Some studies demonstrate the existence of an important genetic component on number of children and age at first child using data from the Danish Twins registers (Kohler et al. 1999; Kohler and Rodgers 2003; Rodgers et al. 2008). Moreover, new developments on molecular genetics show the importance of specific gene variants on reproductive and fertility behaviour (Guo et al. 2008; Guo et al. 2006; Daw and Guo, 2011).

There are two main ways in which genetic dispositions may influence human fertility. First, there can be a direct effect on physiological characteristics (e.g., fecundity, age at menarche, age at menopause). Second, biological predispositions may affect the processes of decision-making and life course planning, consciously and subconsciously (Kohler et al., 2006). Many human traits and behaviours result from both genetic and environmental factors. Genes provide the potential for a trait, but environmental conditions determine whether that potential will be realized. To understand GxE interactions, we must evaluate the estimated heritability of a trait in a particular environment. Using historical cohorts of twins in Denmark, Kohler et al. (1999) show how the heritability on number of children changed across time, changing from zero for some periods to a moderate level of around .40. In particular, they found that heritability increased dramatically in historical periods when social norms on fertility and family size became less stringent. Based on their findings, a central hypothesis is that heritability of fertility behaviour is higher when women and men have more freedom in determining their fertility behaviour. The extent to which people can modify their fertility behaviour depends on socio-cultural and economic circumstances. To test this hypothesis and to further gain knowledge on what kind of environmental factors are most important for

human fertility behaviour we need to undertake heritability analyses of twins in different environments.

Aim of study and contribution to the literature

The aim of this study is extend existing research on this topic – carried out in Denmark – to a highly different environmental context. Our primary goal is to first replicate, but then extend the aforementioned Danish findings to the United Kingdom. We will investigate the heritability of fertility behaviour by examining the age at first birth, number of children and childlessness. Specifically, we will compare the heritability in different cohorts, and compare within cohorts of twins born in diverse social backgrounds.

To our knowledge no such heritability analyses have been undertaken of twins in other countries than Denmark. Therefore, a primary goal is to extend and replicate these Danish findings. The UK is an interesting candidate to study because the British fertility regime differs from the Danish. In addition, the UK is less of a homogeneous country than Denmark. Both in terms of larger geographic differences, but also in terms of population, as the UK is ethnically more diverse. Moreover, the UK can be characterised as a less egalitarian society than Denmark, which may also lead to larger differences in environments for twins. We therefore anticipate that heritability estimates may differ between twins born and raised in different countries, but also between twins raised in different parts of a particular country and coming from a different social background.

Data and methods

We will use data from TwinsUK, the biggest adult twin registry in UK. It consists of 12,000 twins used to study the genetic and environmental aetiology of age related complex traits and diseases. The sample consists of twins aged 16 to 100 with approximately equal numbers of identical (MZ) and non-identical (DZ) twins. The sample is predominantly formed by women (80%) for historical reasons. Detailed collection of physical, physiological, behavioral and lifestyle data is carried out via twin, and the completion of self-administered questionnaires, which are sent to the volunteers for completion every six months. Details information concerning fertility outcomes (number of children, age at births, spacing between children) are available. Moreover the sample include detailed medical information on the reproductive history. This includes age at menarche, age at menopause, pregnancies outcomes (including still births and miscarriages).

By facilitating comparisons between monozygotic (MZ) and dizygotic (DZ) twins, twin registers represent some of the best resources for evaluating the importance of genetic variation in observed traits (Boomsma et al., 2002). Heritability represents the amount of variation in a trait due to genetic factors. We will use standard models from genetic epidemiology to disentangle the proportion of variance due to genetics from the influence of shared context. Using both genetic additive models (ACE) and dominant models (ACDE), we aim to estimate heritability (h^2) and the role of common context (c^2) in determining age at first birth, number of children and childlessness at the end of reproductive life. Estimation are conducted through Structural Equation Modelling (SEM). For a detailed description of the methods, we refer to Kohler et. al, 1999. Previous research indicate that genetic influences on fertility are mediated by the dynamic social context in which individual live. We aim to

extend the previous works by examining the heritability of fertility traits on different strata of UK population. In particular, we will conduct separate analysis by ethnic group, socio-economic status and birth cohorts. This will permit us to have a first insight on the interaction between genetic endowment and social context on fertility behavior.

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