Gene-Environment Interaction in the Intergenerational Transmission of Health: The Case of Asthma

Owen Thompson*

Abstract

Recent economic research has found strong linkages between parent and child health, but the mechanisms underlying these intergenerational effects are not well understood. Motivated by biomedical research that has increasingly focused on interactions between genetic and environmental health determinants, this paper investigates how the importance of genetic health transmission mechanisms vary by environmental conditions in the case of pediatric asthma, a highly prevalent chronic condition with substantial long term socioeconomic effects. Specifically, I study how differences in the strength of asthma transmission within biological versus adoptive parent-child pairs further differ across families of different SES levels. The basic finding is that the aggregate importance of genetic transmission mechanisms varies greatly by SES, with genetic mechanisms playing a much larger role in higher SES families. For example I find that among parent-child pairs where the parent is a college graduate, asthma transmission is approximately 75% weaker for adoptees than for similar biological children, implying a dominant role for genetic transmission. In contrast, among the children of parents without a college degree, asthma transmission rates are virtually identical across biological and adoptive children, implying a modest or non-existent role for genetic transmission.

*University of Wisconsin - Milwaukee, thompsoo@uwm.edu

Introduction

Economists have a longstanding interest in the extent to which social and economic status is transmitted across generations, and a recent strand of this literature explores linkages between parental and child health (for examples see Conley & Bennet 2000; Currie & Moretti 2007; Trannoy et al. 2010; Venkataramani 2011; and Bhalotra & Rawlings 2011, 2012). Such linkages are of interest to economists both because health is an important socioeconomic outcome in its own right, and because health, particularly childhood health, is a well established proximate cause of essential economic outcomes such as income and educational attainment.

With respect to the mechanisms underlying health transmission, most serious health conditions are known to have significant genetic and environmental components, but contemporary medical research has increasingly stressed the importance of interactions between genetic and environmental health determinants. In this framework, the relative importance of genetic predispositions is not a fixed proportion, but rather varies based on the environmental circumstances an individual faces. While intuitive and well supported empirically in most contexts, the gene-environment interaction framework has not been meaningfully incorporated into social scientific research on health transmission.

The present study seeks to begin filling this gap in the literature with respect to a particularly important childhood health condition, asthma. Pediatric asthma is the single most common chronic condition among American children, impacting approximately one in ten children nationally with substantially higher prevalence rates among low income and minority populations (Akinbami 2006). Childhood asthma is a leading cause of missed school days, and has been shown to have significant long term impacts on health, human capital accumulation and economic success (Case et al. 2002; Currie et al. 2009; Fletcher et al. 2010).

It is generally well accepted that gene-environment interactions play a central role in asthma pathogenesis, and identifying specific susceptibility genes and investigating their interactions with various environmental triggers is an active area of medical and epidemiological research. For instance Gilliland et al. (2002) found that in-utero and early life exposure to tobacco smoke decreased lung function and increased asthma symptoms significantly more among children with a null allele at the GSTM1 gene locus than for those without the null allele, while Lee et al. (2004) found that exposure to particulate matter increased asthma risk significantly more for children who were GSTP1 homozygotes than for carriers of the Val 105 alleles. Koppleman (2006) and Ober & Yao (2011) provide insightful reviews of this literature.

Rather than focus on specific genetic loci, the present paper attempts to quantify the importance of gene-environment interactions in the intergenerational transmission of asthma by building on an alternative approach that is well established in the economic literature on intergenerational mobility. Specifically, I first estimate the aggregate genetic component of intergenerational asthma transmission by comparing the strength of transmission in a national probability sample of over 2,000 adoptees versus a matched sample of biological children. Several influential economic studies have used adoptees to isolate genetic transmission mechanisms for non-health related characteristics (see Plug 2004; Björklund et al. 2006; and Sacerdote 2007, among others), but the approach has been only sparsely applied to intergenerational health transmission.[1] Next, I measure the extent to which these estimates of genetic transmission vary by family background measures, specifically parental education and household income.

The basic finding is that the aggregate importance of genetic transmission mechanisms varies greatly by

[1] Exceptions include Sorensen et al. (1988) and my own earlier research (Thompson, forthcoming) using the same data as the present study.

SES, with genetic mechanisms playing a much larger role in higher SES families. For instance, I find that among parent-child pairs where the parent is a college graduate, asthma transmission is approximately 75% weaker for adoptees than for similar biological children, suggesting a dominant role for genetic transmission. In contrast, among the children of parents without a college degree, asthma transmission rates are virtually identical across biological and adoptive children, suggesting a modest or non-existent role for genetic transmission. These results are present when using propensity score methods to account for differences in the characteristics of families with adopted and biological children, are robust to using various measures of asthma status and SES, and placebo tests suggest they are not driven by non-random matching of adoptees.

The remainder of this preliminary draft describes the utilized data, discusses my empirical approach, and presents preliminary results.

1 Data

Data is drawn from the National Health Interview Survey (NHIS), an annual nationally representative survey conducted by the Centers for Disease Control. In its current design, which began in the 1998 wave, the NHIS first randomly selects approximately 40,000 households for participation, and then randomly selects one adult and one child (if present) from each participating household to complete an extensive health related survey instrument. In most cases, the selected adult and child are a parent-child pair, and by pooling the 1998-2012 waves of the survey I am able to create a working data set that contains detailed information on asthma status for over 120,000 parent-child pairs. The selected adult answered the survey questions directly, while information about the selected child was provided by a "responsible adult family member," typically the surveyed parent.

While the NHIS did not intentionally seek out adopted children for participation, the very large size of the combined annual samples led to the incidental inclusion of approximately 2,100 adoptees. I identify adoptees as cases where the selected adult listed their relationship to the selected child as "adopted parent." I am able to identify and exclude cases where the relationship between the selected adult and child is extended family member, older sibling, step parent or foster parent, as well as cases where the selected adult reports being the selected child's adoptive parent, but another parental figure in the household is listed as a blood relative of the child. This rules out, for instance, situations where a biological parent's partner or an extended family member formally adopts a child.

The primary shortcoming of the NHIS adoptee sample is that no details of the adoption process are reported, for instance the age at which the child was adopted or the administrative and institutional details of the placement. However, the NHIS adoptee sample is large relative to much of the existing literature, especially in the US.[2] It is also noteworthy that the NHIS adoptees are derived from a national probability sample, whereas many previously used adoptee data sets are to a large degree convenience samples.

All of the utilized NHIS waves include indicators of whether each parent and child has ever been formally diagnosed with asthma, and this is the primary asthma measure used here.[3] Additionally, the 2003 and

[2] For example Das & Sjogren (2002) work with a sample of 126 adoptees; Plug (2004) uses information on 610 adoptees; and Sacerdote (2002) uses two samples of adoptees, one with a size of 300 and the other with a size of 128.

[3] Also available are indicators of whether they have had an asthma attack in the past 12 months, and whether they have been admitted to an emergency room or urgent care center for an asthma attack in the past 12 months, and I plan to incorporate these measures into future drafts of the paper.

2008 waves of the NHIS asked a more detailed set of questions regarding asthma care and management. These included whether the parent and child had spoken to a health professional about long term asthma management, whether they had ever taken preventative asthma medications, and whether they had made changes to their home, work or school environments to improve asthma symptoms. Several commonly used measures of SES are also included in the NHIS, including parental education levels and household income-to-needs ratios.

A final germane feature of the NHIS is that it contains a large set demographic and health related covariates, including the age, race, and gender of both generations as well as self rated health, health insurance coverage status, and information on health behaviors and birth weight. Combined with the large number of observations, this makes the NHIS particularly well suited for implementing matching methods, as discussed in more detail below.

2 Specifications and Threats to Study Design Validity

My basic empirical approach is to simply estimate regressions of the following form separately for adoptive and biological parent-child pairs of various SES levels:

$$Asthma_i^1 = \alpha + \beta\, Asthma_i^0 + \varepsilon_i \tag{1}$$

where $Asthma_i^1$ indicates whether the child from family i is asthmatic by the measures described above and $Asthma_i^0$ indicates the same for the parent from family i. The coefficient β provides a measure of asthma transmission strength by estimating the percentage point change in the likelihood of a child reporting asthma which is associated with having a parent who has asthma. My primary interest is in seeing how this parameter differs across biological versus adoptive children in families of different SES levels.

Studies using adoptees to isolate genetic effects face two major threats to their validity: differences in the characteristics of adoptive versus biological parents and children, and nonrandom matching of adoptive parents and children. I address these issues in turn.

Families that include adopted children typically differ from those that include only biological children along myriad dimensions, many of which could plausibly effect asthma transmission. The problem is demonstrated in the first two columns of Table 1, which respectively report the means of several potentially important characteristics in the adoptive and biological families of my NHIS sample. The table shows that adoptive parents tend to be older, whiter, and in better general health than their biological counterparts, and are also considerably less likely to be a current smoker and to be married. Additionally, adoptive children are older, less likely to be white or to currently lack health insurance, and are much more likely to have had a birth weight under 2,500 grams and than biological children.

To account for these differences, I use a propensity score matching approach that selects a group of biological children with characteristics closely resembling my sample of adoptees. The NHIS data is well suited for such an approach, because it contains over 125,000 biological parent-child pairs to use as potential control observations and a rich set of variables to match on.

I estimate propensity scores with a probit specification that models the probability of adoptive status as a function of the following characteristics: the age, race and gender of both parents and children; the martial

status, self-rated health, and smoking status of parents; the health insurance status and low birth weight status of children; and the family's current region of residence. Using this propensity score, I match adoptive parent-child pairs to their three nearest neighbors in the biological sample, and drop non-matched biological observations.[4]

The third column of Table 3 reports means for this matched sample of biological parent-child pairs. With the partial exception of child race, the matched biological sample is very similar to the adoptive sample in terms of demographics and health measures. Because the set of matching variables is not fully comprehensive, there could still remain important differences between the adoptive sample and the matched biological sample, but the close resemblance of the two groups is none the less encouraging.

The second major threat to study validity is the nonrandom placement of adoptive children into families. Specifically, it is generally plausible that healthier adoptive parents are, on average, able to adopt children with more favorable genetic health profiles. If asthma is one of the dimensions along which such non-random placement occurs, then there may be a substantive degree of similarity between adoptive parents and children with respect to genetic predispositions for asthma despite the lack of direct genetic linkages, which could severally bias heritability estimates. It is worth noting that because my primary interest is in how genetic transmission varies by SES, non-random placement is only problematic to the extent that it differs by the education or income of adoptive parents. However, such variability in non-random placement cannot be ruled out, and some method of assessing the issue is desirable.

To do so, I conduct a placebo test by re-estimating my main models with asthma status replaced by age and sex adjusted height. Height is a commonly used health marker, but is also known to be overwhelmingly genetic in contexts like the contemporary US where basic nutritional needs are met near-universally. The logic underlying this placebo exercise is therefore that if the matching of adoptive parents and children in the NHIS sample is orthogonal to their respective health profiles, then no significant intergenerational correlations in height should be observed among adoptive parent-child pairs. Any substantial departure from this expectation would raise serious concerns about adoptees being selectively placed on the basis of health. Of course, a finding that adoptees are placed randomly with respect to height does not conclusively rule out the possibility that they are placed non-randomly with respect to asthma, but I still feel that this placebo test is a valuable exercise.

3 Results

The first two columns of Table 2 report OLS estimates of Equation 1 for all biological and adoptive parent-child pairs, respectively, in my working matched sample. Asthma is measured as having ever been diagnosed with the condition, and to increase precision I control for the same demographic and health related variables used to generate propensity scores, though omitting these controls does not meaningfully change the parameter values, as expected given the high degree of covariate balance.[5] The results in Column 1 indicate that among biological children, having a parent who has been diagnosed with asthma increases the prob-

[4] In future versions of the paper I plan to add additional covariates and use a more systematic method of selecting a matching estimator and matched sample.

[5] The results are also very similar if logit or probit models estimated via maximum likelihood are used instead of OLS. Because it is not conceptually clear what broader population the matched sample of biological children is intended to be representative of, I do not apply sampling weights.

ability that they will be diagnosed themselves by 16.5 percentage points.[6] Among adoptive children, the analogous increase in the probability of diagnosis is 11.5 percentage points, a reduction of 30.2%. Subject to the caveats discussed above, this reduction can be interpreted as evidence that approximately 30% of the intergenerational transmission of asthma occurs via genetic mechanisms.

However, if gene-environment interactions are an important component of asthma transmission, then this single point estimate may mask important heterogeneity in the strength of genetic transmission: more than 30% of transmission may occur via genetic mechanisms for populations facing particular sets of environmental circumstances, while less than 30% does so for populations facing other sets of environmental circumstances. One broad marker of environmental circumstances that has been of interest to economists studying child health is SES, typically measured using parental education or income (Currie 2009). Given this, the remaining columns of Table 2 report asthma transmission rates among biological versus adoptive parent-child pairs, but does so separately for families in which the parent had no more than a high school diploma, where they had attended some college but not graduated, and where they were a college graduate.[7] The corresponding percent reductions among adoptees is also reported for each of these groups.

The results provide evidence that the role of genetic transmission mechanisms does indeed vary by family background. In particular, among families where the parent had no more than a high school diploma or had attended some college but not graduated, transmission strength is virtually identical among adoptive versus biological parent-child pairs. This suggests that genetic asthma transmission is negligible in low to moderate parental education. In strong contrast, among families where the parent was a college graduate transmission strength is over 75% weaker among adoptees than among biological children, suggesting a predominant role for genetic transmission mechanisms.

In addition to parental educational attainment, the NHIS contains information on household level income to needs ratios. An advantage of this measure over parental education is that it measures SES at the household level, whereas education is only reported for the parent who was randomly selected to complete the survey, and it is possible the other parent (when present) has a different level of education. Income to needs ratios also have the advantage of being measured semi-continuously, allowing me to investigate non-linearities in future drafts of the paper. The main disadvantage of income to needs ratios is that due to refusals they are missing for approximately 15% of the sample, and in addition approximately 25% of the sample is assigned a top-coded value of 5. I replace missing income to needs observations with imputed values developed by Scehnker et al. (2009), and stratify the sample into families with income to needs ratios below two, ratios between two and five, and ratios of five or greater.

Results are shown in Table 3, and broadly mirror the education based results in Table 2. In particular, for low income families the effect of parental asthma on child asthma falls by 19.1% among adoptees relative to biological children (from 17.3 to 14.0 percentage points), while among middle income families the estimated role of genetic transmission is 21.5%. In contrast, the asthma transmission rate in the high income families falls by 62.4% among adoptees, from 17.2 to 6.5 percentage points.

As discussed above, a major concern with the all adoptee based research designs is that adoptive children are placed with parents in a non-random fashion that leads to genetic similarity between adoptive parents and children despite the absence of direct genetic linkages. If adoptive parents and children in the NHIS share

[6] From a base child prevalence rate of 14.8% this represents an 111% increase in the probability of diagnosis..

[7] The NHIS reports highest grade completed through 12 years, but then only reports education categorically as 1-3 years of college or college and beyond. Because very few adoptive parents have less than 12 years of education, I collapse the continuous portion of the reported education levels into the described categories.

health related genetic profiles, then we might observe positive correlations in their heights, even though height is an almost exclusively genetic trait in the current context. Table 4 reports results from a placebo exercise in which the analysis from Table 2 is repeated but with asthma status replaced by height.[8] Reassuringly, the heights of biological parent-child pairs are strongly correlated for all SES levels, but among adopted parent-child pairs there is no statistically significant association in height, and indeed the point estimate is slightly negative. While not conclusive, these results are consistent with the assumption that adoptive parents and children are not meaningfully matched along health dimensions in this sample.

[8] Unfortunately the NHIS did not begin collecting height data for children until the 2008 version of the survey, and then did so only for children ages 12-17, resulting in substantially reduced sample sizes for the height models. Height is measured in inches and adjusted for age and gender.

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Table 1: Means by Adoption Status

	Adoptive Sample	Full Biological Sample	Matched Biological Sample
Parent Age	46.76	36.81	45.91
Parent White	0.80	0.76	0.79
Parent Married	0.71	0.66	0.69
Parent Self-Rated Health	2.24	2.08	2.25
Parent Current Smoker	0.15	0.21	0.15
Child Age	9.49	8.33	9.49
Child White	0.64	0.76	0.70
Child Uninsured	0.05	0.10	0.06
Child Low Birth Weight	0.12	0.08	0.12
Observations	2,080	127,892	5,235

Table 2: Asthma Transmission by Adoption Status and Parental Education

	All Levels		Parent High School or Less		Parent Some College		Parent College or Beyond	
	Biological	Adoptive	Biological	Adoptive	Biological	Adoptive	Biological	Adoptive
Parent Ever Diagnosed with Asthma	0.165***	0.115***	0.161***	0.168***	0.140***	0.149***	0.179***	0.044
	(0.024)	(0.029)	(0.040)	(0.058)	(0.037)	(0.054)	(0.039)	(0.040)
Percent Decline Among Adoptees	-30.2%		4.5%		6.7%		-75.4%	
Observations	5,235	2,080	2,113	651	1,467	584	1,605	840

Dependent variable is an indicator of whether the child has ever been diagnosed with asthma. All models control for the age, race and gender of both parents and children; the martial status, self-rated health, and smoking status of parents; the health insurance status and low birth weight status of children; and the family's current region of residence. Robust standard errors in parentheses. *, ** and *** denote statistical significance at the 1%, 5% and 10% levels, respectively.

Table 3: Asthma Transmission by Adoption Status and Household Income

	Income/Needs < 2		2 ≤ Income/Needs < 5		Income/Needs ≥ 5	
	Biological	Adoptive	Biological	Adoptive	Biological	Adoptive
Parent Ever Diagnosed with Asthma	0.173***	0.140**	0.149***	0.117***	0.172***	0.065
	(0.036)	(0.057)	(0.039)	(0.044)	(0.047)	(0.050)
Percent Decline Among Adoptees	-19.1%		-21.5%		-62.4%	
Observations	1,746	537	2,161	871	1,328	672

Dependent variable is an indicator of whether the child has ever been diagnosed with asthma. All models control for the age, race and gender of both parents and children; the martial status, self-rated health, and smoking status of parents; the health insurance status and low birth weight status of children; and the family's current region of residence. Robust standard errors in parentheses. *, ** and *** denote statistical significance at the 1%, 5% and 10% levels, respectively.

Table 4: Height Transmission by Adoption Status and Parental Education

	Parent High School or Less		Parent Some College		Parent College or Beyond	
	Biological	Adoptive	Biological	Adoptive	Biological	Adoptive
Parental Height	0.195*	-0.091	0.324***	-0.039	0.398***	-0.078
	(0.100)	(0.163)	(0.090)	(0.114)	(0.088)	(0.110)
Percent Decline Among Adoptees	-146.6%		-121.1%		-119.7%	
Observations	237	80	179	73	208	83

Dependent variable is child's height in inches adjusted for age and gender. All models control for the age, race and gender of both parents and children; the martial status, self-rated health, and smoking status of parents; the health insurance status and low birth weight status of children; and the family's current region of residence. Robust standard errors in parentheses. *, ** and *** denote statistical significance at the 1%, 5% and 10% levels, respectively.