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Parenting and Reproductive Stoppage in the Psychopathology for Recurrence Risk of Autism Spectrum Disorder

Michael Beenstock

Abstract

During 1950 to 1975 autism was considered to be psychopathological in origin, brought on by ‘bad’ mothering in particular. Subsequently, research into the etiology of autism spectrum disorder (ASD) has been dominated by the neurodevelopmental paradigm according to which ASD is genetic or biological in origin. In the present paper population cohort data for Israel are used to show that recurrence risk of ASD (when more than one child has ASD) depends on three parent-related phenomena. First, it varies inversely with the ‘veil of ignorance’ defined as the period of time younger siblings were raised before their elder sibling was diagnosed. Second, it varies inversely with the ‘shadow of ASD’ defined as the period during which parents raised their child with ASD before younger siblings were born. Third, recurrence risk is greater if parents knew the ASD status of their child before conceiving their next child. These three effects, which are shown to be consistent with a behavioral theory of ASD, are inconsistent with neurodevelopmental theory. They suggest that what parents know or do not know about the ASD status of their child is salient for recurrence risk in their subsequent children.

Keywords: reproductive stoppage, natural experiment, recurrence risk, psychopathology of ASD, neurodevelopmental theory, population cohort data, diagnostic timing

1. Introduction

“Many people made a mistake in going from a statement which is undoubtedly true – that there is no evidence that autism has been caused by poor parenting – to the statement that it has been disproven. It has not actually been disproven. It has faded away simply because, on the one hand, of a lack of convincing evidence, and on the other hand, an awareness that autism was a neurodevelopmental disorder of some kind.”

Sir Michael Rutter [1].

Rutter, a pioneer of the neurodevelopmental paradigm for autism spectrum disorder (ASD), was referring to the early belief that the etiology of autism was behavioral, induced by “refridgerator” mothers in particular and poor parenting in

general. His reference to “poor parenting” was intended as a criticism of theories due to Kanner and Bettelheim, who claimed that bad parenting plays a key role in the etiology of autism. Kanner [2], who identified autism as a separate pathology, observed that few of his 11 patients had warm-hearted parents, and subsequently noted that his patients “were exposed from the beginning to parental coldness, obsessiveness and a mechanical type of attention to material needs only.” Moreover, it is as if they had been “kept in refrigerators which did not defrost.” [3] Bettelheim [4] took this argument further, and attributed autism exclusively to the behavior of parents in general, and to “refrigerator mothers” in particular. Indeed, psychoanalytical theory continues to inform the treatment of ASD in some parts of the world, especially in France, Argentina and South Korea [5].

Kanner eventually took exception to Bettelheim’s position, noting that “at no time have I pointed to parents as the primary post-natal source of pathogenicity.” [6] Subsequently, this developmental psychopathology was discredited following the scandal which broke out after Bettelheim’s death [7, 8] and was abandoned in scientific research. Indeed, behavioral research into autism disappeared altogether.

Rutter was also referring to the dominance of the neurodevelopmental model, pioneered by Rimland [9], in the empirical study of ASD, according to which its etiology is mainly genetic or biological and is also environmental. However, environmental factors exclude parents and what occurs within families, and refer instead to exposure to pollution and related factors that might harm brain development [10].

In the present paper we report empirical results for the recurrence risk of ASD, which are inconsistent with the neurodevelopmental model, and for which behavioral interpretations are suggestive. These results are generated by a natural experiment [11] in which the age at which children with ASD are diagnosed serves to randomize their parents’ state of mind at the time they decided to have further children. Some parents had further children before their previous child was diagnosed with ASD, while other parents had further children after diagnosis. The former parents could not have engaged in reproductive stoppage [12] because they did not know (for sure) that their child had ASD. The latter parents, by contrast, consciously refrained from reproductive stoppage.

The two types of parents are different in other ways too. Parents who could not have engaged in reproductive stoppage raised their next child under a “veil of ignorance”, which lasted until their previous child was diagnosed with ASD. By contrast, parents who refrained from stoppage raised their next child in the “shadow of ASD”, which lasted from when previous children were diagnosed until their younger siblings were born. Neurodevelopmental theory attaches no importance to the veil of ignorance and the shadow of ASD, or whether parents conceived younger siblings before or after their previous children had been diagnosed. Parents under the veil of ignorance might be less stressed than other parents. On the other hand, parents in the shadow of ASD gained experience in raising children with ASD. If recurrence risk depends empirically on the durations of the veil of ignorance and the shadow of ASD, this begs a behavioral interpretation in which stressed parents may be more likely to raise children with recurrence risk, when experienced parents are less likely.

The main hypothesis of interest is whether recurrence risk of ASD depends on phenomena such as the veil of ignorance and the shadow of ASD. Since recurrence risk is only observed if parents do not engage in reproductive stoppage, these phenomena are to some degree self-selected. If so, their causal effect on recurrence risk would not be identified. To establish causality an auxiliary hypothesis is proposed in which reproductive stoppage depends on when elder siblings are diagnosed with ASD. If the latter is independent of recurrence risk, it serves to

randomize the veil of ignorance and the shadow of ASD, which are related to reproductive stoppage, and thereby identify their causal effects on recurrence risk.

We use population cohort data for Israel to study reproductive stoppage and to show that the risk of ASD recurrence among younger siblings of children diagnosed with ASD depends causally on the durations of the veil of ignorance and the shadow of ASD.

2. Theory

2.1 Reproductive stoppage

Let C_{it}^* denote a latent or index variable ([13], p. 888), which measures parents' desire in family i in the general population to have a further child when their previous child is aged t . C_{it}^* is hypothesized to depend on a vector of observable covariates (X_i) including the existing number of children, their gender mix, the age of mothers and perhaps fathers, their ethnicity, schooling and economic status etc. Parents have unobserved preferences for children denoted by c_i . Parents may penalize small birth gaps in the interest of birth-spacing, but the penalty, denoted by $g_i(t)$, tends naturally to zero with the birth gap (t).

The latent variable model for the general population may be written as:

$$C_{it}^* = X_i\beta + c_i - g_i(t) \quad (1)$$

where β is a vector of parameters to be estimated. Let C_{it} denote a zero–one dummy variable, which equals 1 if parents conceive their next child when their previous child is aged t . This event occurs when C_{it}^* turns positive as illustrated in **Figure 1** where C^* is measured on the vertical and the age of the previous child (t) is measured on the horizontal axis. Schedule A plots the relation between C^* and t in Eq. (1), and is drawn for positive c and $X\beta = 0$. Schedule A is naturally negative at the origin unless parents wish to conceive straight away, and it tends to c as the birth gap (t) increases. Parents conceive when C^* turns positive, when their child is aged t_0 , which varies inversely with their preference for children (c) and directly with $g(t)$. If c is negative they will not conceive at all because C^* remains negative.

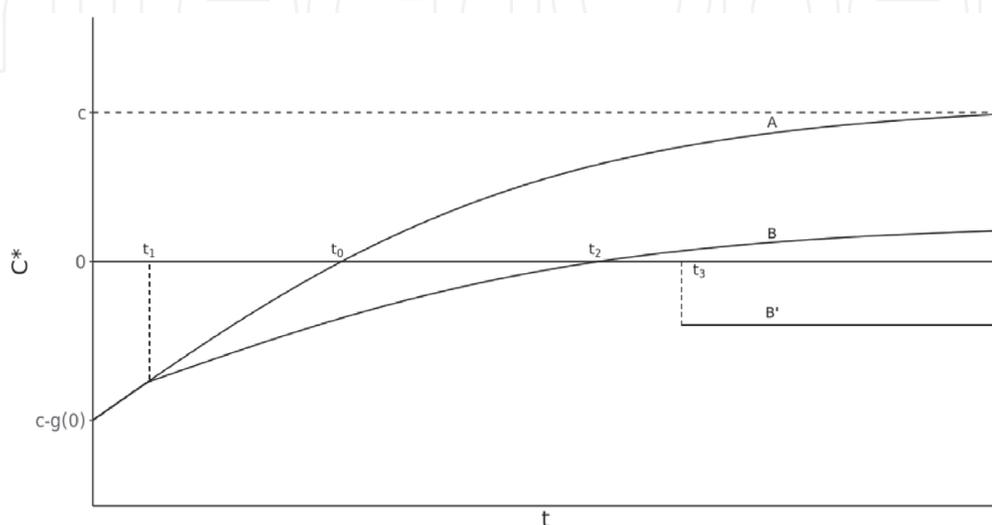


Figure 1.
 Conception timing of younger siblings.

Eq. (1) applies to the general population, which we adapt for parents of children with ASD. We introduce two new unobservable phenomena in addition to c and g , which apply specifically to parents of ASD children. When their index child is born, parents are unaware that they are no longer part of the general population. However, they gradually realize that their child has developmental difficulties, denoted by $d(t)$, which varies directly with age (t). Even before their child is diagnosed with ASD, they might consider reproductive stoppage. Parents also vary by their resilience [14], or their ability to cope with crises denoted by r , which may be positive or negative. We add to Eq. (1) $r_i - d_i(t)$, which may be positive for resilient parents.

Schedule B in **Figure 1** refers to parents of ASD children. At first, it is congruent with schedule A, but after their child is aged t_1 , at which parents begin to worry about their child's developmental problems, it lies below schedule A, where the vertical difference between the schedules equals $r - d(t)$. This distance naturally increases with t . In **Figure 1** schedule B becomes positive at t_2 , so the parents of children with developmental difficulties will tend to delay conception relative to the general population. Of course, schedule B might never become positive, in which case parents engage in reproductive stoppage.

Suppose that the child is diagnosed with ASD when he or she is aged t_3 . This would induce a discontinuous increase in d , which lowers schedule B as in schedule B'. The parents depicted in schedule B, who conceived when their child was aged t_2 , regret their decision. However, it is too late and they could not have known. Matters would have been different had their child been diagnosed prior to t_2 . Note that if parents are sufficiently resilient and their desire for children is sufficiently strong, schedule B' may lie above schedule B, in which case parents conceive further children despite the ASD status of their child. We refer to this by "informed" non-stoppage, and the solution at t_2 by "uninformed" non-stoppage.

This theory implies that observationally similar parents (with the same X) in the general population will have different probabilities of natural stoppage. It also implies that observationally similar ASD parents will have larger probabilities of reproductive stoppage than in the general population. Finally, it implies that observationally similar parents of ASD children have different probabilities of non-stoppage because they differ by their resilience (r), their desire for children (c), their reaction to developmental difficulties and to diagnoses of ASD (d). It also means that observationally similar parents in the general population cannot be compared with the parents of ASD children, because β in the general population may differ, and because r and d do not apply to the general population. Finally, the probability of non-stoppage varies directly with the age at which ASD is diagnosed, and informed non-stoppage is less probable than uninformed non-stoppage.

In summary, the probability of non-stoppage is predicted to depend through β upon the observable covariates (X) including age at diagnosis. Eq. (1) is estimated using data for families with ASD children only; data for the general population are not used.

2.2 The veil of ignorance and shadow of ASD

Suppose A and B are two observationally similar families. Their first children have ASD, and their second children were born three years afterwards. The only difference is that ASD was diagnosed in family A at 2 years and in family B at 8 years. This gives rise to three differences between families A and B. First, when family A decided to have their second child, they already knew about the ASD status of their first child. They decided against reproductive stoppage in having their second child. Matters are obviously different in family B; they had their second child without knowing about the ASD status of their first child. Second, the

younger sibling in family A was raised in the 'shadow of ASD'. His parents had a year's experience raising a child with ASD before their second child was born. Family B obviously had no such experience before their second child was born. Third, the second child in family B was raised until 5 years under a 'veil of ignorance', which ended when his elder sibling was diagnosed. During the veil of ignorance family B might have been concerned about developmental delays in their child, but they did not know for sure that their child would eventually be diagnosed with ASD. In family A the veil of ignorance is zero and the shadow of ASD is a year. In family B the veil of ignorance is 5 years and the shadow of ASD is zero.

According to the neurodevelopmental paradigm of ASD, recurrence risk should be the same for families A and B, because parents' knowledge about the ASD status of their index children plays no role in the neurodevelopmental model. Neurodevelopmentalists might argue, however, that family A was more genetically predisposed to ASD recurrence than family B. Family A's child was diagnosed sooner because his ASD were more severe than B's. That is why A's child was diagnosed more quickly. This argument would predict that recurrence risk should be greater in family A than in family B. Suppose, however, that their recurrence risk differs, and that recurrence risk in B-type families is greater than in A-type families. We suggest three behavioral reasons why this might arise. First, family A is positively self-selected because it decided against stoppage. Parents in family A decided to go ahead despite the risk, either because they were more resilient and self-confident of coping with this risk, or because they suspected that the risk of recurrence is relatively low in their family. Either way, this reduces recurrence risk in family A relative to family B. Second, family B had five years to raise its second child under the veil of ignorance, whereas family A raised its second child entirely in the shadow of ASD. If knowledge of ASD empowers family A to mitigate the risk of recurrence, this would further reduce recurrence risk in A-type families relative to B-type families. On the other hand, if knowledge imperils rather than empowers, A-type families who are fearful of ASD might raise their second child less successfully relative to B-type families who are unaware of ASD. This might increase recurrence risk in A-type families relative to B-type families.

The empower-imperil dichotomy is related to self-fulfilling and self-defeating theories in social psychology [15], dating back to Thomas' Theorem [16]. Family A's knowledge of ASD may become a self-fulfilling expectation if parents believe and fear that ASD will recur in their younger child. If, instead, family A uses its knowledge and experience with ASD to mitigate recurrence risk, the expectation of ASD is self-defeating. During the veil of ignorance, family B has no knowledge of ASD. If knowledge empowers, recurrence risk among B-type families is expected to vary directly with the veil of ignorance. The converse is expected if knowledge imperils.

3. Methodology

3.1 Reproductive stoppage

Two empirical methodologies are considered for estimating β in Eq. (1). If $r + c - d - g = u$ is assumed to have a logistical distribution, β may be estimated by logit using data for C. For informed non-stoppage, the relevant population consists of parents who conceived further children after the date of diagnosis of their index child. For uninformed non-stoppage, the relevant population consists of parents who conceived further children before this date of diagnosis. These two populations may be combined by controlling for the age of diagnosis of the index child. Parents

are less likely to have further children if their index child is diagnosed sooner rather than later.

The second methodology is based on survival analysis focusing on the age of the index child when and if parents conceived their next child. Specifically, a Cox proportional hazards model may be estimated for these purposes. The second methodology [17, 18] is more ambitious than the first [19], because it professes to explain the timing of conception or birth and not merely whether stoppage occurred or not. We prefer the first method to the second because more ambitious methods are generally less robust. For example, Hoffmann et al. [17] assume that birth hazards are strictly proportional to all the covariates in their model, even though this assumption is not essential for testing hypotheses about non-stoppage. They also compare parents of ASD children with parents in the general population, a between-group comparison, instead a within-group comparison in which the parents of ASD children who had further children are compared with parents who had no further children.

Because the data used in the present study end in December 2012, fertility is right-censored; parents of index children who had no further children by December 2012 might have had children subsequently. Hence, censoring artificially increases stoppage even controlling for age of mothers in December 2012. If mothers' age in December 2012 exceeds 45 years, fertility is ascertained and is not censored. A radical solution to the censoring problem would be to ignore diagnoses made after 2004 under the assumption, for example, that parents must have stopped if younger siblings are not born within 8 years. An alternative solution, which avoids discarding data, is to assume that the probability of censoring varies inversely with mothers' age in December 2012. Since this probability is likely to vary nonlinearly with age in December 2012, we estimate this censoring effect as a spline ([13], p. 199). We also use splines to estimate other potentially nonlinear time related variables, such as mothers' age and the age at diagnosis of index children.

If C equals one (non-stoppage), the number of children may be larger or smaller. Just as observationally similar families might stop or not depending on what is not observed (u), so might they choose to have different numbers of children if they do not stop absolutely. Since the number of younger siblings of index children has the character of count data, which take discrete but limited values such as 0, 1, 2, etc. we suggest the use of count data methods [20] to test hypotheses about relative stoppage in which the dependent variable is $C_i = 0, 1, 2$, etc. Specifically, we use "zero-inflated" Poisson regression (ZIP) where the probability of absolute stoppage ($C = 0$) is enlarged according to a complementary log log (CLL) model for the probability of absolute stoppage, and where u is assumed to have a Poisson distribution ([13], p 861; [21]). ZIP embodies the intuition that to have any further children is a harder decision than to have more or fewer further children. This specification combines absolute and relative stoppage, where the former is expressed through zero inflation, and the latter by count data regression.

According to ZIP, the probability of having no further children is:

$$\begin{aligned}
 P_i(0) &= \lambda_i + (1 - \lambda_i) \exp(-\mu_i) & (2) \\
 \lambda_i &= 1 - \exp[-\exp(X_i\gamma)]. \\
 \mu_i &= \exp(Z_i\theta).
 \end{aligned}$$

where λ denotes the CLL probability of having no further children, X are covariates in the CLL model, $\exp(-\mu)$ is the Poisson probability of having no further children, and Z are covariates in the Poisson model. Since $P(0)$ is the probability of absolute stoppage, it varies directly with λ and inversely with μ . CLL is a nonlinear transform of the logit model since $\exp(X\gamma)$ equals the log odds ratio.

Relative stoppage occurs when parents who refrain from stoppage have fewer further children. The ZIP probability of having positive numbers of children ($C > 0$) is:

$$P_i(C > 0) = (1 - \lambda_i)\mu_i^c \exp(-\mu_i) \frac{1}{C!} \quad (3)$$

Suppose for family i the CLL and Poisson probabilities of absolute stoppage are 0.305 ($= \lambda$) and 0.223 ($= \exp(-\mu)$) respectively so that the probability of absolute stoppage, $P(0)$, is 0.46 (as in our data). These probabilities imply that $\mu = 1.5$, i.e. family i is expected to have 1.5 further children. The ZIP probability of having one further child is 0.232 and having two further children is 0.174. Hence, ZIP has inflated the probability of having no further children from 0.223 to 0.46, and it has deflated the Poisson probability of having positive numbers of further children by a factor of $1 - \lambda$.

The expected value of the number of further children given that it is positive equals:

$$E(C > 0) = \frac{(1 - \lambda)\mu}{1 - P(0)} = \frac{\mu}{1 - \exp(-\mu)} \quad (4)$$

which varies directly with μ and does not depend on λ . In summary, absolute stoppage varies directly with λ and inversely with μ , and relative stoppage varies inversely with μ .

3.2 Recurrence risk

As in Sandin et al. [22] and Beenstock et al. [23], we use population cohort data to estimate logit models for ASD recurrence in which the covariates include standard variables, such as the ages of parents and their ethnicity. We supplement these variables by three additional variables. The first is a dummy variable ('informed') that equals 1 if the younger siblings of index children were conceived or born after the index child was diagnosed, and zero otherwise. If parents who refrain from reproductive stoppage are positively selected, the coefficient of 'informed' is expected to be negative (smaller recurrence risk). If they are negatively selected, the coefficient is expected to be positive. According to the neurodevelopmental model, the coefficient is expected to be zero.

The second variable is the duration of the veil of ignorance, which is measured by the age of younger siblings when index children were diagnosed. The veil of ignorance is zero, of course, if 'informed' = 1. If knowledge imperils, recurrence risk is expected to vary inversely with the veil of ignorance; ignorance is bliss. According to the neurodevelopmental model, the coefficient on the veil of ignorance is expected to be zero.

The third variable is the duration of the shadow of ASD, which is measured by the date of birth of younger siblings minus the data of diagnosis of the index child. If knowledge empowers, experience in raising children with ASD may help parents raise their further child more effectively, in which case recurrence risk is expected to vary inversely with the shadow of ASD. If, instead, knowledge imperils, recurrence risk is expected to vary directly with the shadow of ASD. Knowledge is expected to imperil when parents who refrain from stoppage are negatively selected. According to the neurodevelopmental model, the coefficient on the shadow of ASD is expected to be zero.

If parents who refrained from stoppage are negatively selected, it might be expected that for them knowledge imperils, in which case recurrence risk would vary directly with the shadow of ASD. If, instead, they are positively selected, their knowledge might be expected to empower them to mitigate the risks of ASD recurrence. Therefore, estimates of the coefficients on ‘informed’ and the shadow of ASD are unlikely to be independent.

The study of recurrence risk has typically focused on immediate younger siblings. In the present study, we also attach importance to higher order siblings. ASD may not recur among immediate younger siblings, but it may recur among higher order siblings. Inevitably, estimates of recurrence risk and its determinants, may be biased if the incidence of ASD recurrence among higher order siblings is ignored. This bias will be smaller in countries where fertility is low. The bias would be zero if parents limited their fertility to two children. Matters are different in our empirical application for Israel where fertility is high. In our study, families supply more than one observation for estimating recurrence risk. For example, a family with 8 children supplies 7 observations if their firstborn is diagnosed with ASD.

The use of data for all younger siblings raises two statistical concerns. First, the outcomes of younger siblings from the same family are unlikely to be independent; they certainly cannot be treated as the independent outcomes of younger siblings from different families. They share the same parents, the same index child, and they share each other. Consequently, we cluster standard errors of parameter estimates by family ([13], p. 586). Second, we estimate family specific effects that capture familial phenomena that might induce recurrence risk ([13], chapters 11 and 17). These phenomena may be neurodevelopmental or genetic, but they may also be behavioral. Whereas clustering picks up interactions between siblings, specific effects pick up patterns related to families.

Another difference is that, as in the case of Eq. (1), we use censoring methods instead of discarding observations, which are potentially censored. Our data are obtained from administrative records in Israel up to December 2012. Younger siblings born, for example, in 2009 might not have been diagnosed with ASD by December 2012. However, their contribution to recurrence risk estimates is censored since they might have been diagnosed with ASD in 2013 and beyond. Some investigators assume that it takes 8 years for ASDs to be diagnosed [24], and would exclude younger siblings born after 2003. This radical solution to censoring typically discards many observations. In any case, we show below that 8 years is not long enough. Instead of discarding data, we assume that the probability of censoring varies inversely with younger siblings’ age in December 2012. Siblings who were teenagers in December 2012 are uncensored.

Apart from censoring there are several covariates that are related to time, e.g., the age of mothers when their index child was born, age at diagnosis of index children, year of diagnosis, veil of ignorance and shadow of ASD. These time-related variables are not expected to have linear effects. For example, mothers’ fecundity at age 40 is naturally smaller than at age 30. Also, the probability of censoring is expected to vary nonlinearly with the age of younger siblings in December 2012. Therefore, we estimate these relationships as splines ([13], p. 199).

4. Population cohort data

The study group comprises the younger siblings of children diagnosed with ASD in Israel during 1984 to 2012. The outcome of interest is whether ASD recurred among these younger siblings. Since 1981, families of children diagnosed with ASD have been eligible for benefit from Israel’s National Insurance Institute (NII).

Applications for benefit are processed rapidly (within about two months) and benefits are back-dated to the date of diagnosis, provided the application was lodged within 12 months of diagnosis. Consequently, the date of diagnosis is recorded. These data have been matched using the Population Registry and personal id numbers to the parents (and step parents) and siblings (and half siblings) of the children diagnosed with ASD. Dates of conception are approximated by dates of birth minus 9 months. Hence, we are able to determine whether index children were diagnosed before the conception of their younger siblings, during their pregnancy, or after their birth.

Details regarding administrative data sources, diagnostic criteria, the study population, as well as data tabulations etc. may be found in Beenstock, Levine and Raz [23], who used these data in a previous study. The study population comprises 9572 cases of ASD diagnosed during 1984 and 2012, involving 9117 families. Hence, there are 455 cases of recurrence risk. However, in 88 recurrences younger siblings were diagnosed before their older siblings, leaving 367 recurrences according to birth order. Judging by the proximity in diagnoses of these 88 cases, we suspect that attention was drawn to elder siblings once their younger siblings were diagnosed. Since almost all cases of ASD in Israel are known to NII [25], these data constitute population cohort data, which in contrast to survey data and clinical samples, are likely to be free of sample selectivity.

Table 1 shows that 4219 parents of children with ASD had no further children by December 2012. However, many families had several further children, reflecting the high rate of fertility in Israel. The same applies to the birth orders of index children, of which 4076 were firstborns. In many families, however, index children are not firstborns. Indeed, **Table 1** shows that ASD may suddenly occur after the birth of several children. These data may be unique in enabling the estimation of birth order effects on stoppage and related phenomena. Finally, **Table 1** reports years in which the diagnoses were made, and the number of cases for population subgroups, of which ultra-orthodox Jews account for 12 percent of the population, and non-Jews (mainly Arabs) who account for 20 percent of the population. See Raz et al. [25] for further discussion of the incidence of ASD among these sub-groups.

The age at which autism spectrum disorders (ASD) are diagnosed has a wide variance. Some children are diagnosed quickly, before they are 3 years old, while others are diagnosed in their teens. **Figure 2** shows that in Israel although 40 percent were diagnosed by the age of four, the age distribution has a long tail, and more than 10 percent were diagnosed after they were ten years old. This means that many parents raised the younger siblings of children who are eventually diagnosed with ASD without being aware of the ASD status of the latter. It also means that many parents did not engage in reproductive stoppage because they were unaware of the ASD status of their index child when their subsequent children were conceived or born. **Figure 2** also shows that initially girls are diagnosed more quickly than boys.

The first column of **Table 2** refers to the proportion of parents who refrained from stoppage by ethnicity and year of diagnosis. The second and third columns refer to the proportions of children whose parents were informed or not when they were born and conceived. Note that because parents who refrained from stoppage had several further children (**Table 1**), they might have been informed for some of these children, especially higher order siblings, and uninformed for others, especially immediate siblings.

Figure 3 plots the distribution of the duration of the veil of ignorance for uninformed parents. It has a mode at 2.5 years with a long right-hand tail. For some, the veil of ignorance exceeds ten years. During this period, parents raised their further children without knowing that their index child would eventually be diagnosed with ASD.

Number diagnosed	9572
Number of families	9117
Number of younger siblings	
0	4219
1	2974
2	1222
3	378
4	151
5	91
6	33
7	28
8+	21
Index Year of Diagnosis	
1989–1995	217
1996–2001	1622
2002–2006	2534
2007–2012	4744
Index Birth Order	
1	4076
2	2588
3	1336
4	563
5	265
6	131
7	66
8	30
9	23
10	18
11+	21
Ethnicity	
Jews	8539
Ultra-orthodox Jews	935
Non-Jews	500
Mixed-marriages	28

Table 1.
Study group characteristics.

Figure 4 plots the distribution of the shadow of ASD. It has a mode of a year and long right-hand tail. Some parents reared their children with ASD for as long as ten years and more before their younger siblings were born. Indeed, there is much similarity between the distribution of the shadow of ASD in **Figure 4** and the veil of ignorance in **Figure 3**. Both distributions have natural minima at zero, and do not

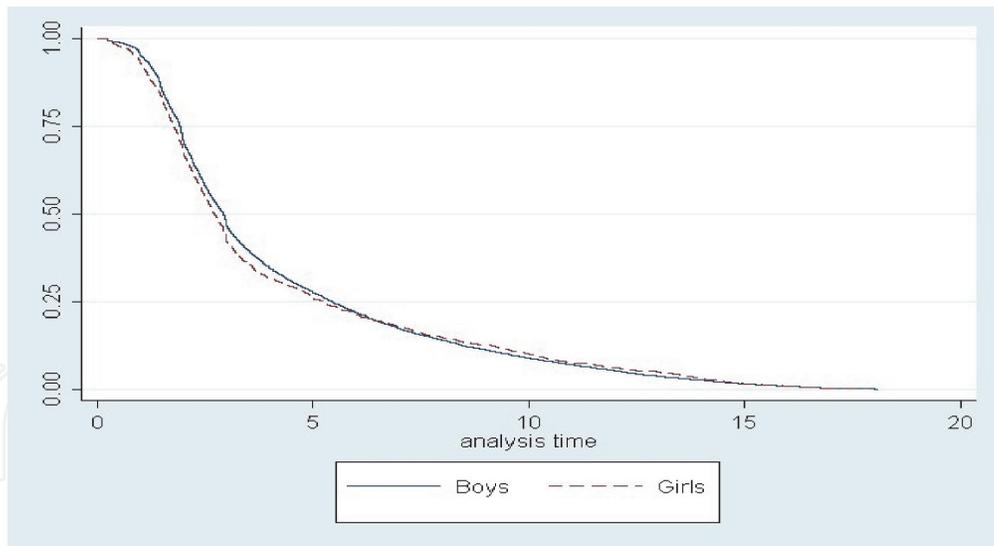


Figure 2.
 The age distribution of ASD diagnoses in Israel.

No-Stoppage	Total	Informed	Uninformed
All	54%		
Jews	4618	54%	2690
Non-Jew + Half	280	53%	174
Ultra-Orthodox	706	76%	466
Not Ultra-Orthodox	4192	52%	2398
Year of diagnosis			
1989–1995	124	96	56
1996–2001	1019	815	436
2002–2006	1428	1016	741
2007–2012	2327	937	1764

Table 2.
 Non-stoppage: Informed and uninformed.

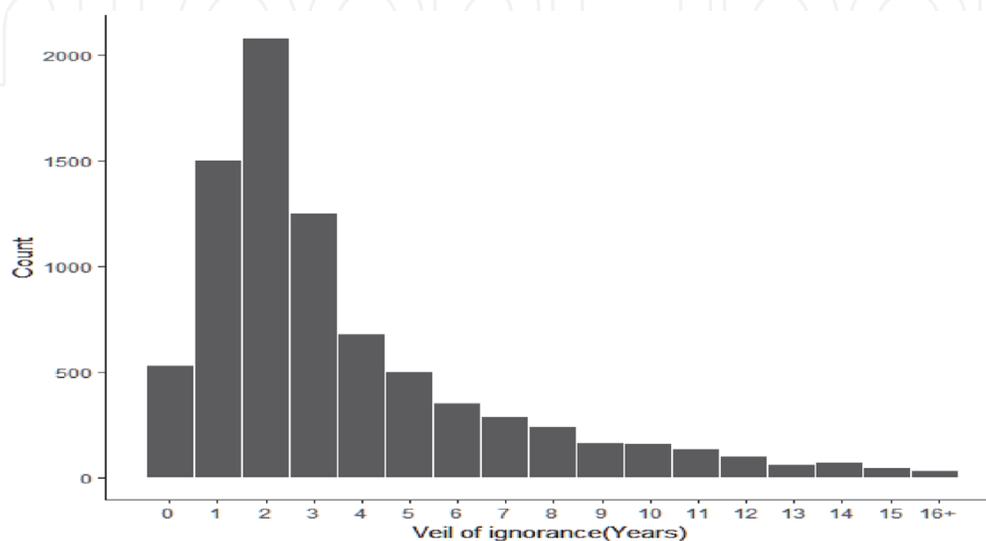


Figure 3.
 The distribution of the veil of ignorance.

overlap. If the veil of ignorance is zero, the shadow of ASD must be positive. If the shadow of ASD is zero, the veil of ignorance must be positive by definition.

Rates of recurrence risk are reported in **Table 3**. Overall recurrence risk is 4.53 percent. However, for diagnoses of index children made prior to 2000 recurrence risk was lower (3.8%). Recurrence risk among the ultra-orthodox is smaller (3.2%)

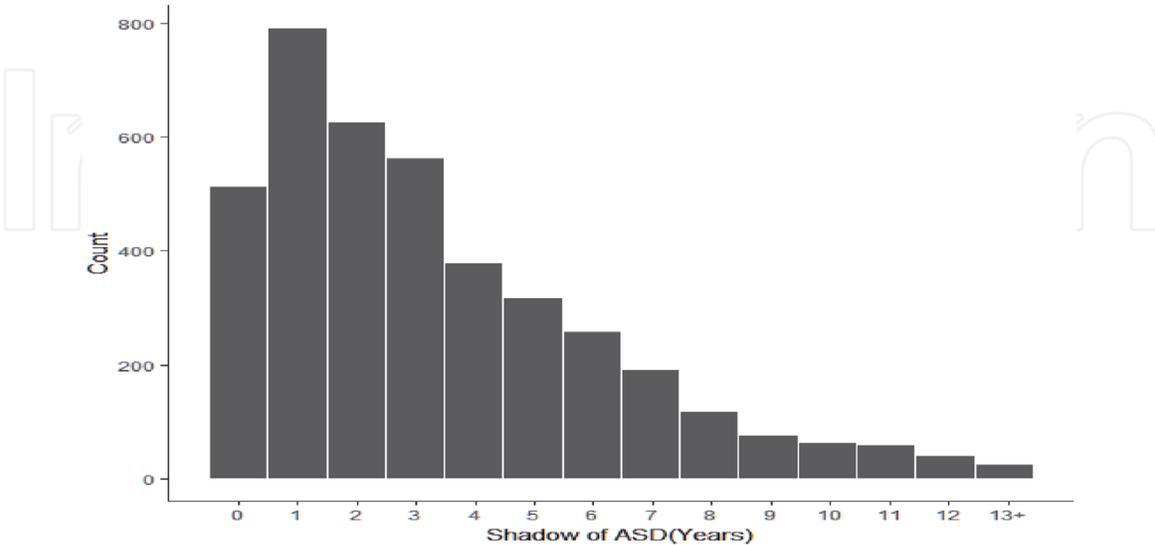


Figure 4.
The distribution of the shadow of ASD.

	Recurrence Risk
All	0.0453
Before 2000	0.0380
Ultra-orthodox	0.0320
Boy - boy	0.0642
Girl - girl	0.0321
Girl - boy	0.0862
Boy- girl	0.0185
Informed	0.0367
Informed - from conception	0.0350
Uninformed	0.0476
Uninformed - from conception	0.0468
Veil of Ignorance	
< 1.25 years	0.0669
1.25-3.5 years	0.0572
> 3.5 years	0.0447
Shadow of ASD	
< 1.32 years	0.0439
1.32-3.33 years	0.0572
> 3.33 years	0.0278

Table 3.
Rates of recurrence risk.

because (as explained below) their fertility is higher. Recurrence risk also depends on gender mixes. The largest risk (8.62%) occurs when the index is a girl and her younger sibling is a boy. The smallest risk (1.85%) occurs when the index is a boy and his younger sibling is a girl.

Recurrence risk is a percentage point larger if parents are uninformed. For example, using conception as a reference point, recurrence risk for the informed is 3.5% and for the uninformed it is 4.68%, which seems to suggest that knowledge empowers more than it imperils. Recurrence risk also appears to vary inversely with the veil of ignorance, and perhaps to vary inversely with the shadow of ASD. The former appears to suggest that ignorance is bliss, and the latter appears to suggest that experience in raising children with ASD helps parents mitigate recurrence risk.

5. Results

5.1 Absolute stoppage

The results in **Table 4** refer to the probability of parents of children with ASD having further children (non-stoppage) by the end of the study period in December 2012. Model 1 refers to all parents regardless of being informed or not. It shows that non-Jews (Arabs) and ultra-orthodox Jews are more likely to engage in non-stoppage than Jews in general, while mixed couples (Jews and Arabs) behave similarly to Jews in general. A number of variables capture the effect of target family size. Non-stoppage varies inversely with the birth order of the index child. If the index child has a twin, the probability of non-stoppage decreases by more than what is implied by birth order. Several studies have shown that there is male preference in Israel [26, 27]; parents are more likely to have further children if their children are all girls. **Table 4** suggests that male preference does not apply to ASD families. Finally, the presence of other disabled siblings in the family increases stoppage, but this effect is not statistically significant.

Several time-dependent variables in **Table 4** have been estimated by splines, all of which are statistically significant. The direction of their effects are indicated by +/- signs in **Table 4**. For example, older mothers are less likely to engage in non-stoppage. Mothers who were older in 2012 were more like to have not stopped, implying that the fertility of younger mothers in December 2012 is right-censored, as expected. Finally, the probability of non-stoppage varies directly with age of diagnosis, implying that ignorance about the ASD status of their children reduces the probability of stoppage.

Models 2 and 3 decompose the non-stoppage models for informed (at birth) and uninformed parents. Models 2 and 3 refer to the probability of informed and uninformed stoppage respectively in the population as a whole. The covariates that are statistically significant (or not) in Model 1 are also statistically significant in Models 2 and 3. However, their odds-ratio coefficients are different. On the whole, their deviations from unity are larger for the uninformed than the informed. For example, the OR coefficient for non-Jews is 1.62 in Model 3 and 1.34 in Model 2, and the coefficients for twins are 0.67 and 0.25 respectively. Age at diagnosis is omitted from Model 2 because it is not relevant for informed parents, but it is extremely statistically significant in Model 3. This effect ranges between -2 at two years to 1.8 at five years and 2 at ten years. Therefore, the size effect of age at diagnosis on the odds ratio for stoppage is large and negative, especially over the range of 2-5 years.

Model 4 refers to uninformed parents according to age at conception rather than age at birth. The OR coefficients in Model 4 should therefore be compared with their counterparts in Model 3. On the whole, the OR coefficients are similar in terms

	1 Informed + Uniformed		2 Informed from birth		3 Uninformed from birth		4 Uninformed from conception	
	OR	P-value	OR	P-value	OR	P-value	OR	P-value
Intercept	8.5079	0.0380	0.5022	<0.0001	0.2999	0.2987	0.6654	0.6901
Mixed	0.5434	0.1742	0.4403	0.1190	0.5861	0.3036	0.7826	0.5832
Non-Jew	1.4855	0.0007	1.3376	0.0107	1.6157	0.0001	1.5044	0.0004
Ultra-Orthodox	4.4353	<0.0001	2.5784	<0.0001	3.6689	<0.0001	3.9408	<0.0001
Twins	0.3482	<0.0001	0.6697	0.0007	0.2470	<0.0001	0.2456	<0.0001
Index birth order	0.7557	<0.0001	0.8333	<0.0001	0.8525	<0.0001	0.8176	<0.0001
Disabled sibling	0.7791	0.1420	0.9239	0.6515	0.8296	0.3430	0.8593	0.3987
No males	1.0261	0.7550	1.0280	0.7238	1.0076	0.9329	1.0523	0.5370
year of diagnosis	0.9156	0.1567			1.0165	0.8142	1.0060	0.9228
Mother age at birth of index	Spline -	0.0308	Spline -	<0.0001	Spline -	<0.0001	Spline -	<0.0001
Mother age in 2012	Spline +	<0.0001	Spline +	<0.0001	Spline +	0.0217	Spline +	0.0126
Age at diagnosis	Spline +	<0.0001			Spline +	<0.0001	Spline +	<0.0001
Log likelihood	-4929.6		-4886.6		-4053.7		-4722.3	
Observations	9087		9087		9087		9087	

Note: OR odd ratio. Direction of splines indicated by +/-.

Table 4.
Logit models for absolute non-stoppage.

Age at diagnosis	Model 1	Model 3	Model 4
2.5	0.45	0.19	0.29
5	0.55	0.62	0.73
7	0.63	0.66	0.77

Notes: Jews excluding ultra-orthodox, dummies = 0, year of diagnosis 2010, mother age = 30. Model numbers refer to Table 4.

Table 5.
Non-stoppage and age at diagnosis.

of their p-values and their size effects. However, because these estimates are precise, the differences between them are statistically significant.

In **Table 5** we use the results in **Table 4** to calculate the probability of non-stoppage for observationally similar families, which differ by the age at which their index child was diagnosed. According to Model 1, the probability of non-stoppage varies directly with age at diagnosis, as expected. The probability of non-stoppage increases from 0.45 when age at diagnosis is 2.5 years to 0.63 at 7 years. For uninformed parents at birth (Model 3) these probabilities are initially much smaller

(0.19 instead of 0.45) but are slightly larger at 7 years (0.66 instead of 0.63). For uninformed parents at conception the probabilities of non-stoppage are larger as expected. Model 2 does not feature in **Table 5** because for informed parents age at diagnosis does not matter.

5.2 Relative stoppage

We use the zero-inflated Poisson model to distinguish between absolute and relative stoppage. As in **Table 4**, we compare families with ASD children who stopped or not, and who had more or fewer further children if they did not stop. The first column in **Table 6** refers to the complementary log log (CLL) component of the ZIP model in which λ refers here to the probability of non-stoppage, and the covariates refer to the X variables hypothesized to affect the logit probability of engaging in absolute non- stoppage, i.e. the probability of having further children after the index child. For example, Non-Jews and ultra-orthodox Jews are more likely to engage in absolute non-stoppage (less likely to engage in absolute stoppage). The second column refers to the Poisson probability (μ) of having 0, 1, 2, etc. further children after the index child, and the covariates refer to the Z variables hypothesized to affect the number of further children. For example, the ultra-orthodox are likely to have $\exp.(0.8299) = 2.3$ further children more than other parents. This means that the ultra-orthodox are less likely to engage in absolute stoppage and less likely to engage in relative stoppage.

In **Table 6** the X and Z covariates for Eq. (2) are almost identical. Covariates that are statistically significant, carry the same signs in the CLL and Poisson models (non-Jews, ultra-orthodox, age of mother, age at diagnosis). An exception is birth order of the index child, which reduces absolute stoppage, but increases relative stoppage. This means, for example, that parents of second children diagnosed with ASD are more likely to stop than parents of firstborns, but the former are likely to have more further children than the latter. Another exception is twins, which increases absolute stoppage but does not significantly affect relative stoppage.

	CLL model		Poisson model	
	Estimate	p-value	Estimate	p-value
Intercept	-0.7409	<0.0001	0.0378	0.2791
Non-Jew	0.3889	<0.0001	-0.4153	0.1892
Mixed			0.2787	0.0001
Ultra- orthodox	0.9184	<0.0001	0.8299	<0.0001
Twins	-0.1186	0.2450	-0.7496	<0.0001
Birth order	0.0800	<0.0001	-0.2051	<0.0001
Disability	-0.0778	0.4457	-0.1729	0.1325
Mother age	Spline -	<0.0001	Spline -	<0.0001
Age at diagnosis	Spline +	0.0084	Spline +	<0.0001
Mother age 2012	Spline +	<0.0001	Spline +	<0.0001
Observations	9087			
Log likelihood	-9664			

Table 6.
Zero-inflated Poisson model for absolute and relative stoppage.

Age at diagnosis is specified in the CLL and Poisson models as is appropriate. The former implies, as in **Table 4**, that the probability of absolute non-stoppage varies directly with age at diagnosis. The latter implies that the probability of having more than one subsequent child also varies directly with age at diagnosis. Hence, both absolute and relative non-stoppage vary directly with age at diagnosis.

In **Table 7**, we use the results in **Table 6** to calculate the effect of age at diagnosis on the probabilities of absolute and relative non-stoppage, where the former refers to the probability of non-stoppage, and the latter refers to the expected value of the number of further children. As expected, both outcomes vary directly with age at diagnosis. The probability of absolute non-stoppage increases from 0.48 when the age at diagnosis is 2.5 years to 0.61 when the age at diagnosis is 10 years, and relative non-stoppage as measured by the expected value of the additional number of children increases from 0.37 to 0.7. Recall that the latter is defined by the probability of having one further child multiplied by one plus the probability of having a second further child multiplied by two etc. Hence, the expected number of children are weighted probabilities, which may be fractions as in **Table 7**.

5.3 Recurrence risk

Our main results are reported in **Table 8** where Models 1 and 2 are logit models for the probability of recurrence risk with common effects and random effects specifications. The latter hypothesizes that individual families have different recurrence risks, whereas the former hypothesizes that different families share common recurrence risks, but recurrence risk for siblings from the same family are correlated. Hence, for Model 1 parameter standard errors are clustered. On the whole, clustered standard errors are smaller than their unclustered counterparts, suggesting that siblings are negatively correlated within families as far as recurrence risk is concerned. This means that ordinary standard errors under-estimate the significance levels of the results. The reported p-values refer to the clustered standard errors for model 1. Since the results of the two models are similar, we focus here on Model 1.

Because most of the variables in **Table 8** were featured in a previous study [23], we focus here on the three new parental variables, which are highlighted in italics. The results of the previous study focused on birth gaps and birth orders of index children and their younger siblings. We reconfirm that short birth gaps (less than 2 years) increase recurrence risk, that recurrence risk varies inversely with the birth orders of younger siblings and the birth orders of index children. Also, recurrence risk is smaller in the non-Jewish population, varies directly with mothers' disability, and younger siblings are censored, as expected, with the probability of censoring tending to zero at 9 years of age. We found no evidence that recurrence risk varies with mothers' age (when her index child was born), nor could we detect a time

Age of index at diagnosis	Probability of stoppage	Expected number of children
2.5	0.72	1.44
5	0.71	1.52
7	0.71	1.61
10	0.73	1.69

Notes: Based on **Table 6**. See notes to **Table 5**.

Table 7.
Age at diagnosis and absolute and relative non-stoppage.

Model	1 Common Effects			2 Random Effects	
	Odds Ratio	SD-cluster	P-value (clustered)	Odds Ratio	P-value
Intercept	0.1706	0.1661	< 0.0001	0.1693	< 0.0001
Female sibling	0.2851	0.1274	< 0.0001	0.2847	< 0.0001
Birth order after index	0.8344	0.0704	0.0102	0.8374	0.0226
Index birth order	0.9244	0.0488	0.1077	0.9251	0.0999
Birth gap < 2	1.4297	0.1363	0.0087	1.4350	0.0090
Female index	1.6112	0.1324	0.0003	1.6094	0.0003
Mother disability	1.6995	0.2273	0.0196	1.7016	0.0217
Ultra-Orthodox	0.7682	0.1674	0.1153	0.7675	0.1058
Non-Jew	0.2294	0.4222	0.0005	0.2294	0.0005
Veil of ignorance	0.8552	0.0286	< 0.0001	0.8547	< 0.0001
Shadow of ASD	0.9300	0.0350	0.0387	0.9830	0.0593
Informed	0.6364	0.1621	0.0053	0.6355	0.0069
Censor	Spline +		< 0.0001	Spline +	0.0024
Observations	8164			8164	
Log likelihood	-1376			-24864	

Table 8.
 Logit model for recurrence risk: Informed at birth.

trend in recurrence risk that might have reflected the positive time trend in the incidence of ASD in the general population [25].

We turn now to the three highlighted behavioral variables in **Table 8**. ‘Informed’ is a dummy variable, which equals 1 if index children were diagnosed before their younger siblings were born and is zero otherwise. The relative risk of ASD recurrence when parents are informed is reduced by slightly more than 30 percent. This effect is statistically significant and its p-value is 0.0053. ‘Shadow of ASD’ refers to the experience (in years) that informed parents had in raising their children with ASD before their younger siblings were born. The estimated coefficient implies that the relative risk of recurrence decreases by approximately 7 percent for each additional year of experience. This effect is very statistically significant since its p-value is almost zero. Finally, ‘veil of ignorance’ refers to the period of time (in years) during which uninformed parents raised the younger siblings of index children before the latter were diagnosed. The estimated coefficient implies that the relative risk of recurrence decreases by about 15 percent for each year of ignorance. This effect is very statistically significant too. Indeed, a likelihood ratio test overwhelming supports the retention of all three variables. However, their inclusion does not significantly affect the parameter estimates of the other variables in **Table 8**.

As mentioned, results for Model 2 are similar to those for Model 1, suggesting that Model 1 is robust with respect to random effects. Family random effects are hypothesized to be normally distributed with mean normalized to zero. The standard deviation of these effects is estimated at 0.588, which implies that recurrence risk for families at the lower 95 percentile is 1.47 percent, and it is 13 percent at the upper percentile. Mean recurrence risk is 4.5 percent. The asymmetry stems from the fact that the standard deviation refers to the log odds ratio. These results suggest that recurrence risk differs widely among families. **Figure 5**, which plots family specific effects expressed as odd ratios, suggests that there are two types of family.

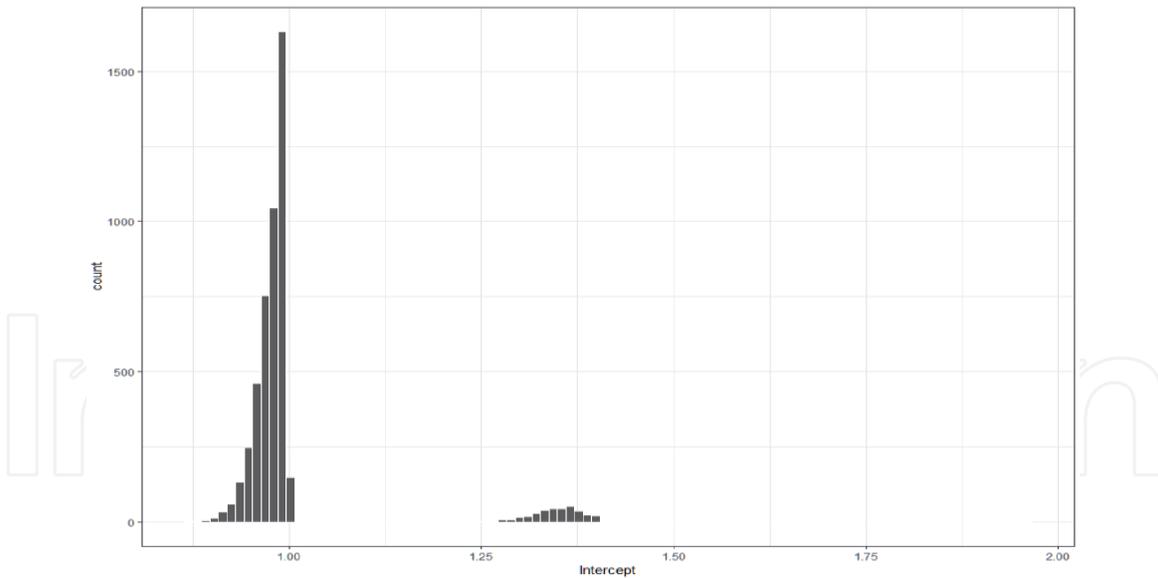


Figure 5.
Distribution of family specific odds ratios.

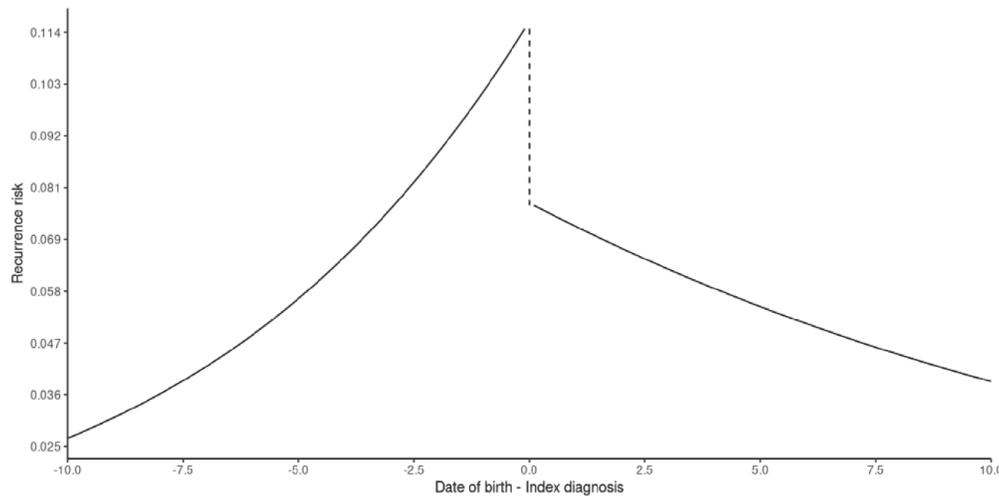


Figure 6.
Recurrence risk and shadow of ASD or veil of ignorance.

The first group has odds ratios that are slightly less than 1, while the second group, which is smaller, has odds ratios that are about 1.3.

In **Figure 6** we plot the relationship, implied by **Table 8**, between recurrence risk (on the vertical axis) and the difference between the birth dates of younger siblings and the dates at which index children were diagnosed (on the horizontal axis). Parents are ‘informed’ if this difference is positive because younger siblings were born (or conceived) after their index siblings were diagnosed. If this difference is negative, parents were ‘uninformed’. Therefore, the shadow of ASD increases to the right of 0 on the horizontal axis, and the veil of ignorance increases to the left. The baseline for recurrence risk is 4.5 percent as in the data because logit models replicate sample means. Notice that the origin for the shadow of ASD is 2.91 percent because informed parents have lower odds ratios according to **Table 8**.

Figure 6 shows that recurrence risk varies directly with the gap between dates of birth and dates of diagnosis. **Figure 6** also shows that recurrence risk varies inversely with the shadow of ASD and the veil of ignorance. At one year, the veil of ignorance reduces recurrence risk from 4.5 percent to 3.87 percent and to 2.03 percent after 5 years. At one year, the shadow of ASD reduces recurrence risk from

4.5 percent to 2.71 percent and to 2.09 after 5 years. The results in **Table 8** refer to “informed” at birth. Since the results are similar for informed at conception, we do not present them here.

6. Conclusion

The opening quotation from Rutter, made in 2010, applies also today. In this paper, we respond to Rutter’s challenge by reporting empirical evidence of three behavioral phenomena in the determination of recurrence risk. Our interpretation of these phenomena in terms of empowerment and imperilment theory, and self-selectivity into reproductive stoppage is less important than their statistical salience. Perhaps other interpretations exist. However, behavioral theory provides axioms, which predicted these effects. By contrast neurodevelopmental theory does not.

The result that recurrence risk is smaller among informed parents is consistent with them being more resilient. This does not mean that they are better parents. It simply means that parents who knowingly or consciously decided against reproductive stoppage are different to parents who conceived before their index child was diagnosed. Nor do we claim that the neurodevelopmental model is false. Indeed, our results are consistent with this model. However, they are not exclusively so. We find that the three behavioral parental phenomena significantly improve predictions of recurrence risk when they are added to the neurodevelopmental model. However, standard neurodevelopmental covariates such as birth gaps and birth orders continue to be statistically significant; they are not superseded by the three behavioral parental phenomena.

Can these behavioral results be confounded by neurodevelopmental effects? This would be the case if the difference between the dates of diagnosis of elder siblings and the dates of conception or birth of younger siblings happened to be correlated with neurodevelopmental phenomena. This difference is positive for uninformed families and negative for informed families. This difference also equals age at diagnosis minus sibling age gaps. There is no reason to suspect that sibling age gaps are directly or indirectly correlated with neurodevelopmental genotypes. However, age at diagnosis might be negatively correlated, if severer cases of ASD are diagnosed more quickly. If so, recurrence risk should vary inversely with age at diagnosis, and birth gaps should have no effect on recurrence risk. Since our results reject both of these predictions, we do not think that they are an artifact of confounding.

Standard neurodevelopmental covariates, such as birth order, might also bear behavioral interpretations. The neurodevelopmental interpretation is that birth order is naturally larger in families that have had more regular children. These families are presumed to be genetically less susceptible to ASD recurrence. A behavioral interpretation might be that parents who have had more experience in raising children are more resilient, which is why recurrence risk varies inversely with birth order. The same applies to covariates such as the ages of parents, which have behavioral as well as neurodevelopmental interpretations. In observational studies results are inevitably ambiguous. On the other hand, whereas most neurodevelopmental covariates have behavioral interpretations, the three behavioral phenomena studied here do not have neurodevelopmental interpretations.

We make a methodological contribution by exploiting the randomness in the timing of diagnoses as a source of natural experimentation. Randomized trials are obviously not feasible because parents cannot be assigned into treatment groups who are informed and controls who are uninformed. By contrast, natural experimentation induced by the timing of diagnosis most probably reveals the same

information with greater reliability provided recurrence risk is sufficiently independent of the timing of diagnosis.

In summary, the Bettelheim Affair blighted behavioral research into the etiology of ASD. However, the distinction should be made between discredited psychoanalytical theories and untested psychopathological theories that are behavioral. We close with some further quotations from Rutter [28]. “At first sight, it might seem that autism is the diagnostic category least likely to require a developmental psychopathology perspective.” However, in reference to grand discredited theories they add, “There is a continuing need to remain skeptical about the new evangelisms that have come to take their place, but equally the imperative must be to replace doubt with programmatic research that truly tests competing hypotheses.” Hopefully, the present paper will be judged in this light.

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Author details

Michael Beenstock
Hebrew University of Jerusalem, Israel

*Address all correspondence to: michael.beenstock@mail.huji.ac.il

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