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Objectives: To describe time trends in the reported number of patients with ASD in Israel and to characterize the demographic features of the reported patients.

Methods: We reviewed the charts of the National Insurance Institute of Israel from 1972 to 2004 for all children with a diagnosis of ASD receiving disability benefits.

Results: A total of 3509 children met the study criteria. Eighty percent were boys and 98% were Jewish. The incidence data showed an increase in the number of cases from zero in 1982–84 and 2 (1.2 per million capita under 18 years) in 1985 to a high of 428 cases in 2004 (190 per million).

Conclusions: This is the first comprehensive study of the incidence of ASD in Israel. According to data derived from official health records, the rate of occurrence of ASD has substantially increased in the last 20 years. Further studies are needed to determine if this is a true increase or if the findings were confounded by external factors, such as recent improvements in diagnostic measures and social stigmas.

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ASD = autistic spectrum disorder

*This article is dedicated to the memory of Dr. Raphael Drachman

Methods

The data for the present study were collected from the records of the National Insurance Institute of Israel. Patients with ASD are eligible for disability benefits from the NII after their diagnosis is confirmed by a professional
committee on the basis of a range of neurological, psychiatric and developmental criteria. We reviewed the NII files for all children with ASD who received disability benefits from 1972 to the end of 2004. Background information such as age, gender, place of residence, nationality, and date of diagnosis was obtained from the medical charts for patients diagnosed before 1998 and from the computerized records for patients diagnosed after 1998.

CASE ASCERTAINMENT
To validate the accuracy and completeness of the NII data, we compared the cases of ASD registries of two non-governmental organizations specifically serving the ASD community: a developmental disabilities clinic in Rishon Lezion, Israel’s fourth largest city, and the Israeli Society for Autistic Children, a public advocacy and voluntary service agency. We found that the NII records included almost 90% of the members of these organizations.

To investigate the relationship between socioeconomic level and risk of ASD in Israel, we calculated the number of cases of ASD in several Israeli cities against the mean number of children under 14 years old who resided there during the study period, as documented in the records of the Israel Central Bureau of Statistics [18]. The socioeconomic levels (I-III) of the cities were derived from the 1995 National Census poverty index (scale of 0 to 20), which takes into account a range of parameters, including household income, educational qualifications, crowding, material conditions, and car ownership [19].

STATISTICAL ANALYSIS
All statistical analyses were performed with standard statistical software (SPSS, Chicago, IL, USA). Differences in the cumulative incidence proportions for ASD across birth cohorts were evaluated with Kaplan-Meir survival curves. To maintain sufficient statistical power, the analytic birth cohorts for each type of ASD were stratified by year of birth, grouped into 2 year intervals. In this manner we were able to discern the relationship of age and year of birth with the cumulative incidence of reported diagnoses.

RESULTS
A total of 3509 children with ASD were approved for disability benefits by the National Insurance Institute between 1972 and 2004. Eighty percent were boys and 98% were Jewish [Table 1]. Age at diagnosis was available for 82.4% of the subjects (n=2895). The number of incident cases increased over time from a few per year in the 1970s and 1980s to less than 62 (30 per million capita under 18 years) in 1995 and in 1996, to 256 (125 per million) in 1997, reaching a high of 428 (190 per million) in 2004, the last year investigated [Figure 1]. The mean age at diagnosis of ASD was 39 months (SD=30.6). The trends in age at diagnosis are shown in Figure 2. Among boys, children diagnosed between 1995 and 1999 (n=845) were significantly younger than children diagnosed between 2000 and 2004 (n=1135) (average 37 months vs. 42 months, P < 0.01). There was no difference in incidence rates over time by socioeconomic level. The diagnostic distribution of young children with ASD by specialty during the years 1982–97 was as follows: 76% diagnosed by developmental pediatricians, 15% by child psychiatrists, 5% in child neurology clinics, and 4% in other assorted specialty clinic settings.

Table 1. Characteristics of children with ASD receiving disability benefits from the National Insurance Institute of Israel (n=3512)

<table>
<thead>
<tr>
<th>Birth year</th>
<th>N</th>
<th>% of total</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1985</td>
<td>197</td>
<td>5.6%</td>
</tr>
<tr>
<td>1985–89</td>
<td>387</td>
<td>11.0%</td>
</tr>
<tr>
<td>1990–1994</td>
<td>741</td>
<td>21.1%</td>
</tr>
<tr>
<td>1995–1999</td>
<td>1298</td>
<td>37.0%</td>
</tr>
<tr>
<td>2000–2004</td>
<td>886</td>
<td>25.2%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Gender</th>
<th>N</th>
<th>% of total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>2815</td>
<td>80.2%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Nationality</th>
<th>N</th>
<th>% of total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jewish</td>
<td>3423</td>
<td>97.5%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Socioeconomic status</th>
<th>N</th>
<th>% of total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low (&lt; 8)</td>
<td>477</td>
<td>13.6%</td>
</tr>
<tr>
<td>Medium (9–12)</td>
<td>1619</td>
<td>46.1%</td>
</tr>
<tr>
<td>High (&gt; 12)</td>
<td>1279</td>
<td>36.4%</td>
</tr>
<tr>
<td>Missing data</td>
<td>134</td>
<td>3.9%</td>
</tr>
</tbody>
</table>

Figure 1. Number and rate (per million capita under 18 years) of children approved for disability benefits due to ASD
This is the first study, to our knowledge, to describe the national incidence of reported cases of ASD in Israel over a period of more than 20 years. The fivefold increase in the annual number of patients eligible for disability benefits for ASD between 1996 and 1998 might be attributable to several factors, such as improvements in screening programs and the development of better techniques for diagnosis of higher-functioning children, as reflected by the increase in the number of university-affiliated child developmental programs in Israel, from 4 in 1982 to more than 30 in 1999 [20]. The rise in incidence of ASD may also be a consequence of the improved diagnosis and reportage made possible by the universal adoption of standard classification systems of mental disorders (e.g., The Diagnostic and Statistical Manual of Mental Disorders). This may also explain the higher average age of the children diagnosed later.

Our estimates were based on claims for benefits filed with the National Insurance Institute, which we assumed represents the true number of cases in Israel. The validity of this method is supported by the findings of an earlier study showing that the prevalence of childhood autism is approximately 20 per 10,000 [21], in agreement with our calculated rates.

The investigation of the relationship between socio-demographic factors and trends in the temporal incidence of autism is complicated by two main factors. First, autism is a heterogeneous disorder, often accompanied by other behavioral problems and disabilities, and its definitions and means of diagnosis have changed over time. Second, it is not clear whether the relationship reflects a link to etiology or a link to case identification, as suggested in earlier studies [22]. A good example is the Arab sector in Israel, where mental health-related disabilities carry a considerable social stigma and families tend to avoid publicizing them. Consequently, there is less awareness of social and health care-related entitlement in the community and fewer advocacy efforts by local social and health workers on issues of disability claims.

The earlier ASD is diagnosed the sooner patients access interventional services and receive a social security benefit, which eases the family's burden of cost for educational and rehabilitative services [2]. This is especially pertinent in Israel, where it is up to the family to identify and mobilize sources of support and funding. This practice, too, supports our rationale that the NII records would include most cases of ASD in Israel, with further corroboration by our comparison of the findings to the records of non-governmental organizations.

The estimated average age at diagnosis of ASD in the UK is 66 months [13], which is considerably higher than the 39 months calculated in our study during similar calendar years. This discrepancy may be attributable to differences in the system of reportage by the social services in the two countries, as well as to basic disparities in patient access to tertiary care health centers, awareness among professionals, and benefit disbursement policies.

The diagnosis of ASD is occasionally delayed because of the variable clinical presentation and lack of clear biological markers [23]. Researchers have reported a delay of 20–60 months between the onset of parental suspicions and the diagnosis of ASD [24]. At the same time, in some cases, it takes the parents 2 to 3 years to internalize and accept the diagnosis of ASD [25].

The male predominance noted in the present study is consistent with the high male-to-female ratio reported elsewhere for autism. It remains unclear if this finding is associated with etiology per se or with the social milieu in which autistic-like behaviors are recognized more successfully in higher-functioning boys than in higher-functioning girls [22].

Although the growing number of reported cases of ASD cases may reflect a true increase in the occurrence of the disorder, it might also be influenced by such confounding factors as improved diagnosis and more astute awareness by both parents and professionals. This growing number may also represent an over-diagnosis due to benefits that are provided to the families and their children by the National Insurance Institute. In addition to an underlying genetic basis predisposing to the development of language and behavioral symptomatology attributable to ASD, environmental triggers that have contributed to the reported increase in prevalence over the past 20 years may also play a role. Well-designed, nationwide investigations using accu-
rate and uniform criteria are needed to verify the role of age and demographic variables in ASD diagnosis in Israel.

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References

Capsule
Paracetamol plus ibuprofen for the treatment of fever in children

Hay and co-authors investigated whether paracetamol (acetaminophen) plus ibuprofen are superior to either drug alone for increasing time without fever and the relief of fever-associated discomfort in febrile children managed at home. Children aged between 6 months and 6 years with axillary temperatures of at least 37.8°C and up to 41.0°C were given advice on physical measures to reduce temperature and the provision of, and advice to give, paracetamol plus ibuprofen, paracetamol alone, or ibuprofen alone. On an intention to treat basis, paracetamol plus ibuprofen were superior to paracetamol for less time with fever in the first 4 hours (adjusted difference 55 minutes), and may have been as good as ibuprofen (16 minutes). For less time with fever over 24 hours, paracetamol plus ibuprofen were superior to paracetamol (4.4 hours) and to ibuprofen (2.5 hours). Combined therapy cleared fever 23 minutes faster than paracetamol alone but no faster than ibuprofen alone. No benefit was found for discomfort or other symptoms, although power was low for these outcomes. Adverse effects did not differ between groups. The authors conclude that parents, nurses, pharmacists, and doctors wanting to use medicines to supplement physical measures to maximize the time that children spend without fever should use ibuprofen first and consider the relative benefits and risks of using paracetamol plus ibuprofen over 24 hours.