Social Adversity and Regional Differences in Prescribing of ADHD Medication for School-Age Children

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ABSTRACT: ***Objectives:*** **To explore whether regional variations in the initiation of attention-deficit hyperactivity disorder (ADHD) medication among school-age children are explained by differences in sociodemographic composition and/or ADHD prescribing practice, especially in children who face social adversity (low parental education and single parenthood).** ***Methods:*** **A cohort of Danish school-age children (ages 5–17) without previous psychiatric conditions (N = 813,416) was followed during 2010–2011 for incident ADHD prescribing in the individual-level Danish registers. Register information was retrieved for both children and their parents. Regional differences were decomposed into contributions from differences in sociodemographic composition and in prescribing practices. Incidence rate ratios (IRR) with 95% confidence interval (CI) of ADHD prescribing were calculated using demographically standardized multivariable Poisson regression models.** ***Results:*** **Compared with the Capital, prescribing rates were significantly higher in regions North and Zealand (IRR, 1.19; 95% CI, 1.08–1.32 and 1.17; 1.08–1.28, respectively) and lower in South (IRR, 0.60; 95% CI, 0.54–0.66). After inclusion of the interaction term (region*social adversity), the multivariable analyses revealed a higher rate for the most disadvantaged children in North (IRR, 2.00; 95% CI, 1.51–2.66) and a lower rate in South (IRR, 0.47; 95% CI, 0.3–0.65). Prescribing rates were the highest for disadvantaged children in all regions, demonstrating the steepest social gradient in North and the smoothest in South. Demographic composition explained little of the variation: 3% for North and 13% for Zealand.** ***Conclusions:*** **Differences in sociodemographic composition explain little of regional variation in incident ADHD prescribing for children. However, large regional differences prevail in prescribing practices for children facing social adversity, indicating that local cultures shape the interpretation and handling of children with ADHD-like behaviors.**

*(J Dev Behav Pediatr 0:*1–12, 2015) **Index terms:** regional variation, ADHD medication, children, social adversity, prescribing practice variation.

The increasing utilization of medicine for attention-deficit hyperactivity disorder (ADHD) in children has raised concerns partly due to known common side effects and potential long-term side effects such as growth suppression.[1] Other concerns include the potential problems of children being treated with ADHD medication without having the disorder per se.[2] The considerable public awareness of ADHD and the fact that the ADHD diagnosis is based on behavioral symptoms and functional impairment[3,4] carry the risk that children are prescribed ADHD medicine due to learning difficulties or frustrations in school settings expressed as behaviors that may be interpreted as ADHD symptoms (behavioral problems).[5,6] Several studies have demonstrated an association between growing up in socially disadvantaged families and ADHD.[7–9] However, observed country-specific and regional variations in the prevalence of children treated with ADHD medication[10–12] may not reflect differences in the prevalence of ADHD but rather differences in the interpretation and handling of behavioral problems in children faced with social adversity.[10,13,14] These differences may involve health care referrals for ADHD symptoms, ADHD diagnostic practice, and the subsequent decision to prescribe ADHD medicines, e.g. methylphenidate and atomoxetine.

A Canadian cohort study has shown that the likelihood of receiving ADHD medication is predicted by social factors, e.g. low maternal education.[15] Similarly, a recent Swedish study[14] has demonstrated that social adversity as measured by low maternal education, single parenthood, and low income (social assistance recipients) predicts a considerable proportion of ADHD medication in school-age children. The authors of the Swedish study observe that the large regional variation in pediatric prescribing of ADHD medications does not follow any obvious

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sociodemographic patterns and may thus reflect regional variation in prescribing practice rather than variations in risk factors for ADHD.

Attention-deficit hyperactivity disorder is a complex psychiatric syndrome considered to be a neurodevelopment disorder with a multicausal etiology covering both hereditary and environmental pathways (biological and social adversities/risk factors).[16,17] Biological adversity includes vitamin D deficiency and fetal exposure to alcohol and tobacco, whereas social adversity includes low maternal education, single parenthood, low income, parental psychiatric disorder, and reduced family cohesion.[16] The hereditary and environmental pathways may, however, be associated such that predisposed children are more likely to be exposed to biological and/or social adversity,[7,17,18] potentially reinforcing the impact of facing social adversity. Furthermore, without specific biological ADHD markers or medical tests,[3,16] children from socially disadvantaged families may be more likely than other children to be diagnosed and prescribed ADHD medicine without having the neurodevelopment disorder.[14,19]

Even in a small country like Denmark with 5.5 million inhabitants, marked regional differences have been observed in the prevalence of treatment with ADHD medication.[11] This regional variation in Denmark may reflect regional differences in the sociodemographic composition and regional variations in prescribing practice.

The aim of this study was to explore whether regional Danish variations in the initiation of ADHD medication (incident prescribing) among school-age children are explained by differences in sociodemographic composition and/or differences in ADHD prescribing practice, especially for children who face social adversity measured by low parental educational level and single parenthood.

MATERIALS AND METHODS

We undertook a register-based cohort study of all Danish children ages 5 to 17 on January 1, 2010 (N = 866,762). The cohort was followed in the Danish nationwide registries containing individual-level information on health (e.g., dispensed prescriptions and hospital diagnosis) and sociodemographic indicators such as highest level of education attained, income, cohabitation status, and region of residence.[20] Denmark is divided into 5 regions responsible for local tasks, e.g. the organization of health care and schooling to some extent.

By means of an encrypted person identifier, each child was linked to its biological parents or caregiving adults/adoptive parents. The inclusion criterion was school-age children without previous psychiatric diagnosis for not mixing up children with and without psychiatric diagnosis as preschoolers. We hypothesize that the latter in particular may be prescribed attention-deficit hyperactivity disorder (ADHD) medication for psychosocial difficulties in school. The following exclusion criteria were used: children not living together with their parents, children without full follow-up information (i.e., who emigrated or died during 2010–2011), and children with missing information on parental education. This resulted in a final study population of 813,416 school-age children (Fig. 1).

To explore prescribing behavior, we focused on incident ADHD prescribing because long-term users of ADHD medication are more likely to reflect caregivers' evaluation of the benefit/adverse effect (and costs) ratio, which may also be socially patterned. Hence, the outcome of interest was the first dispensed prescription of ADHD medicine between January 1, 2010, and December 31, 2011. As expected, the incidence of ADHD prescribing was higher in the source population than in the study population (with the exclusion of risk factors).

Information on dispensed prescriptions was retrieved from the Danish National Prescription Registry, which contains full information on all prescribed medicines dispensed at Danish pharmacies since 1995.[21] Each record includes the person identifier, dispensing date, and Anatomical Therapeutic Chemical (ATC) classification system code[22] of the dispensed medicine along with nonmandatory information on prescribing indication that is not readily applicable for research.[21] We included medications corresponding to the Danish ADHD recommendation for children: methylphenidate (ATC, N06BA04), dexamphetamine (N06BA02), and atomoxetine (N06BA09), assuming that ADHD was the prescribing indication. Information on inpatient and outpatient diagnoses was retrieved from the

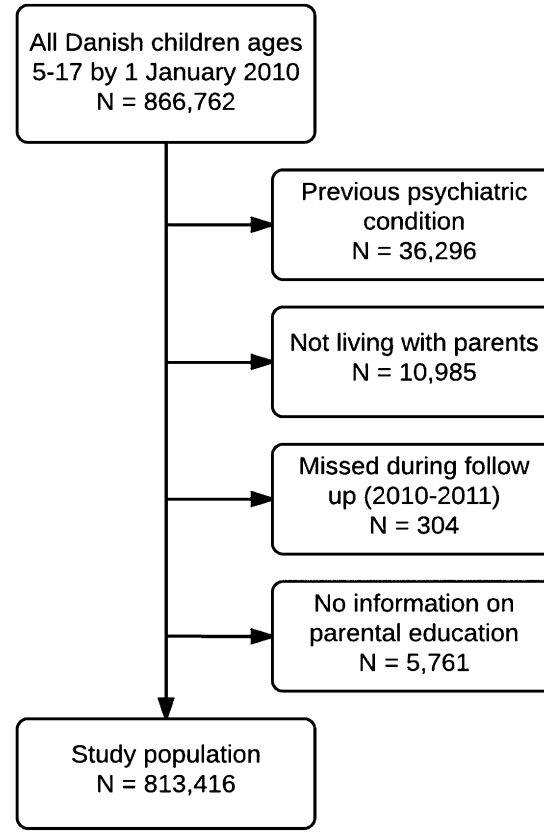

Figure 1. The child study population: flowchart from source population to study population.

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Danish National Patient Registry, which contains information on both psychiatric and nonpsychiatric hospitalizations since 1995.[23] Each record includes information on admission and discharge dates along with the discharge diagnoses according to the International Classification of Diseases, Tenth Revision (ICD-10).[24]

We applied *Parent's highest attained level of education* and *Cohabitation status* as social indicators for measuring the main explanatory variable, social adversity. Parents were defined as the adult(s) with whom the child lives. After the definitions of Statistics Denmark, primary parent was defined as the female parent or the older of 2 persons with caregiver responsibility.

METHODS

We included the following variables as to the child and parent population.

The Child Population

Incident ADHD prescribing during 2010–2011 (yes/no), gender, and age (by January 1, 2010, categorized as 5–8, 9–12, and 13–17 years).

The Parent Population

Highest educational level (categorized as ≤10, 11–12, 13–15, and 16 + years of formal education, calculated as rounded mean of both parents), cohabitation status (single or cohabiting), parental age at the child's birth (categorized as <25, 25–34, 35 + years), region of residence (divided by the 5 Danish regions), ethnicity of primary parent (categorized as Danish-born, immigrants born in Western countries, and immigrants born in non-Western countries), and any previous psychiatric condition during the period 2001–2010 in one or both parents (yes/no). The explanatory variables—*Parent's age at birth of child* and *Ethnicity*—have previously been shown to be associated with ADHD symptoms/medication in children.[15]

Previous Psychiatric Condition

For children as well as their parents, previous psychiatric condition was defined as dispensed prescriptions for drugs used for psychiatric conditions, defined as antidepressants (ATC, N06A) and stimulants (N06B) or any inpatient or outpatient diagnosis (i.e., hospital diagnoses) of mental and behavioral disorders. This includes alcohol abuse (*ICD-10*, F10–19), psychotic and affective disorders (F20–F39), anxiety and phobic disorders (F40–41), mental retardation (F70–79), psychological development disorders (F90–98), behavioral and mental disorders (F90–98), which covers hyperactivity and inattention disorders, and poisoning by hallucinogens and sedatives (T40–43).

As the initiation of pharmacological therapy for ADHD in children and adolescents is a specialist task in Denmark,[25] we assumed that children initiating ADHD medication had been diagnosed in a child and adolescent psychiatric center beforehand. Thus, while children with previous psychiatric conditions were excluded, children diagnosed with ADHD during the observation period (2010–2011) were included. We did not aim to explore regional variation in incident ADHD prescribing among ADHD diagnosed and nondiagnosed children although variation in initiation of ADHD medication may reflect variation in therapeutic and diagnostic practice.[26,27]

Analyses

The cumulative incidence proportion (CIP) of the use of ADHD medicine for 2010–2011 was calculated stratified by region, gender, and age groups. These descriptive analyses were performed for the study population (Table 1) as well as the total source population in Supplemental Digital Content 1, http://links.lww.com/JDBP/A77.

Bivariate Association Between Attention-Deficit Hyperactivity Disorder Prescribing and Parental Educational Level

The bivariate association between incident ADHD prescribing and the highest parental educational level was calculated across each of the remaining explanatory variables.

Bivariate Analyses of the Contribution of the Sociodemographic Composition to the Regional Prescribing Variation

Using the Kitagawa method for decomposing 2 rates,[28] the regional differences in incident ADHD prescribing were decomposed into the contribution of different prescribing practices according to the child's level of social adversity and sociodemographic composition (i.e., the distribution of social indicators). This was done by partitioning the overall difference between the national and regional level in CIP of ADHD prescribing into the components driven by (1) differences in incident ADHD prescribing practice and (2) differences in the demographical distribution of social indicators.

We calculated the CIP level in each region and the difference between the regional and the national CIP level within 8 social adversity levels, i.e. the combination of 4 educational levels and the binary cohabitation status. Similarly, we calculated the sociodemographic composition in each region (in percentage) and the difference between the regional and the national sociodemographic composition, according to the 8 social adversity levels.

The impact of the 2 components for each social adversity level was assessed by standardizing to the distribution of the other component (the average of the national and actual region level). The overall regional-national difference in CIP level attributable to each component was calculated summing up the stratum-specific figures by region and component. Finally, we calculated for each region the proportion of the CIP difference between the national and regional level that could be explained by differences in the sociodemographic composition. The above analyses were not conducted for the Capital region as the differences in the overall CIP between the Capital region and the national level were small and insignificant (Table 1).

Multivariable Analyses of Potential Association Between Social Prescribing Practice and Regional Prescribing Variation

Controlling for other explanatory variables, we used Poisson regression analyses to investigate whether variation in the incidence of ADHD prescribing across region

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Table 1. Descriptive Analysis: Cumulative Incidence Proportion of ADHD Medication Prescribing (CIP[a]) Among Danish Children Ages 5–17[a] During 2010–2011 Across the 5 Danish Regions

		CIP[b] of ADHD Dispensing (‰) by Region					
Gender	**Age, yr**	**National**	**North**	**Middle**	**South**	**Capital**	**Zealand**
Boys	5–8	9.09	12.68	9.34	6.93	7.92	11.61
	9–12	8.56	11.17	8.35	6.09	8.80	10.28
	13–17	6.32	6.70	7.80	3.89	6.09	7.82
Girls	5–8	2.59	4.02	2.46	1.72	2.29	3.73
	9–12	2.91	4.17	2.85	1.60	3.07	3.81
	13–17	3.81	3.93	5.49	1.70	3.30	5.14
Both	All (5–17)	5.54	6.97	6.12	3.59	5.24	7.07

[a]All Danish children ages 5–17 by January 1, 2010: N = 813,416.
[b]Cumulative incidence proportion: Number of incidence dispensed ADHD medications per 1000 children during 2010–2011. Children with previous psychiatric condition and/or not living with their parents are excluded, see Figure 1.
CIP, cumulative incidence proportion.

was associated with different prescribing practice regarding children facing social adversity. We opted to use mulitvariable Poisson regression analyses rather than a multivariable extension of the Kitagawa method (e.g., the Oaxaca decomposition[29]), mainly because we are dealing with rare time-to-event (count) data.

To eliminate the impact of regional differences in the demographic distribution of the social indicators, we standardized the distribution of social indicators to the demographic distribution at national level. Standardization was achieved by first calculating the incidence rate of ADHD prescribing for each level of all explanatory variables, i.e. the variable's stratum-specific number of incident events (dispensed prescriptions) divided by the number of person-years at risk (PYR). The distribution of PYR according to the 8 social adversity levels at each level of the remaining explanatory variables was standardized to the social adversity distribution of the same variable at national level. The standardized number of incident events was estimated by multiplying the "observed" incidence rates in each social adversity level by the standardized PYR (rounded to whole numbers).

Applying these standardized parameters, we conducted sociodemographically standardized multivariable analyses - both stratified by region and in unified analyses with region included in the model. The unified analyses were performed by means of 2 models. In Model I, we explored the regional prescribing variation adjusted for all confounding variables including the combined "social adversity prescribing practice" indicator (8 combinations of educational levels and cohabitation status). To explore regional variation in the social adversity prescribing practice (adjusted for confounders), we included in Model II the interaction between region and the combined social adversity indicator. The incidence rate ratio of ADHD prescribing was estimated with 95% confidence interval, applying the Capital region (the largest population base) as reference category in the unified analyses.

All analyses were performed using STATA 13.

RESULTS

Table 1 shows the cumulative incidence proportion (CIP) of attention-deficit hyperactivity disorder (ADHD) prescribing in 2010–2011 for the study population of Danish children ages 5–17, stratified by gender, age group, and region. Across all regions and age categories, CIP was considerably higher among boys than girls. While CIP tended to decrease with age in boys, the inverse was the case in girls. Marked regional differences were observed with the highest age-specific CIP in regions North and Zealand (6.97‰ and 7.07‰, respectively) and the lowest CIP in region South (3.59‰). No statistically significant difference was found between the Capital region and the national level (5.54‰). CIP for children aged 13–17 was the highest in regions Middle and Zealand.

Table 2 shows a bivariate analysis of the CIP of ADHD prescribing, relating length of parental education with the regional prescribing patterns across the explanatory variables included in the Poisson analysis. Independently of region, CIP decreased with increasing length of parental education, although most pronounced for region North. In region North, 15.5‰ of children from families with the shortest parental education (<10 years) initiated ADHD medication compared with 7.2‰ of those at the next level (10–12 years). In region South, the figures were 5.4‰ and 4.5‰, respectively.

Cumulative incidence proportion decreased with increasing length of parental education for all levels of the other explanatory variables, including parental cohabitation status. The CIP at the lowest parental educational level was almost triple in region North compared with region South. Furthermore, the bivariate analysis showed that CIP decreased with increasing parental age at the child's birth, and that CIP was higher among children of parents with previous psychiatric condition; and considerably lower if parents were born in non-Western countries compared with parents born in Denmark.

Table 3 summarizes the results of the Kitagawa decomposition of regional-to-national differences in the CIP of

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Table 2. Bivariate Association Between Cumulative Incidence Proportion of ADHD Prescribing (CIP[a]) and Length of Parental Education Across Other Explanatory Variables Among Danish Children Age 5–17

	CIP (‰) by Length of Parental Education, yr			
Explanatory Variables	**<10**	**10–12**	**13–15**	**+15**
Region of residence				
All regions/national	9.01	6.32	4.35	2.45
North	15.52	7.18	4.67	3.49
Middle	10.31	6.89	4.80	2.87
South	5.40	4.05	2.81	1.30
Capital	8.08	6.46	4.31	2.50
Zealand	9.85	7.92	5.89	2.25
Child gender				
Boy	12.72	9.13	5.95	3.55
Girl	5.24	3.44	2.69	1.30
Child age group, yr				
5–8	10.99	7.22	4.14	2.48
9–12	9.34	6.69	4.48	2.29
13–17	7.41	5.42	4.43	2.56
Parental age at child's birth				
<20 yr	10.43	8.60	7.25	1.83
20–34	8.51	6.02	4.18	2.60
35+	7.79	5.10	3.98	2.07
Parental psychiatric condition[b]				
No	7.37	5.16	3.67	2.10
Yes	12.18	10.25	7.60	4.70
Parental country of birth				
Denmark	10.29	6.63	4.44	2.47
Western country	11.33	3.76	3.21	2.51
Non-Western country	2.26	1.62	1.59	0.87
Parental cohabitation status				
Single	10.53	8.91	6.61	3.45
Cohabiting	7.44	5.70	3.97	2.32

[a]Cumulative incidence proportion: Number of incident dispensed ADHD medications per 1000 children during 2010–2011.
[b]At least one of the parents has a registered previous psychiatric condition (discharge diagnosis or psychiatric medication).
CIP, cumulative incidence proportion.

ADHD prescribing, splitting up how much differences in respectively social adversity prescribing practices and sociodemographic composition contribute to the overall regional difference. Comparing the 2 regions with the highest CIP, the sociodemographic composition explained 3% of the higher CIP in region North, whereas demographics explained 13% in region Zealand. The sociodemographic composition explained none of the higher CIP in region Middle or lower CIP in region South. Finally, the majority of CIP differences in region North are confined to the lower half of social adversity categories.

Table 4 shows the result of region-specific multivariable Poisson analyses of ADHD prescribing. For all regions, the incidence of ADHD prescribing was considerably lower in girls compared with boys (largest difference in region South) and tended to decrease with increasing parental age at child's birth and with child's age (except for region Middle). The incidence was considerably higher among children of parents born in Denmark compared with parents born in non-Western countries. After controlling for these confounders, the incidence of ADHD prescribing decreased with increasing length of parental education and was higher among children of single parents than cohabitating parents. For both social adversity indicators, this tendency was most pronounced for region North: The educational prescribing gradient in region North was significantly steeper than in the other regions. For example the incidence rate ratio (IRR) among children with 10-12 years of parental education compared with >10 years was significantly higher in North (IRR, 0.59; 95% confidence interval [CI], 0.47–0.73) than in Capital (IRR, 0.93; 95% CI, 0.79–1.11) and South (IRR, 1.02; 95% CI, 0.81–1.29).

Table 5 shows the results of the unified multivariable Poisson regression analyses of the regional variation in ADHD prescribing, controlling for confounding variables (including the joint tendency in social adversity prescribing). Model I demonstrates that regions North and Zealand had significantly higher prescribing compared to the Capital (IRR, 1.19; 95% CI, 1.08–1.32 and 1.17; 1.08–1.28, respectively), whereas region South had a significantly lower rate (IRR, 0.60; 95% CI, 0.54–0.66). After inclusion of the interaction between region and the social adversity indicator, Model II reveals significant regional differences regarding social prescribing practice as to children of single parents with <10 years education (the reference group). Applying the Capital as reference group, prescribing rates for the most disadvantaged children was considerably higher in regions North (IRR, 2.00; 95% CI, 1.51–2.66) and Middle (IRR, 1.30; 95% CI, 1.01–1.68), and a lower rate in region South (IRR, 0.47; 95% CI, 0.4–0.65).

Table 6 displays the interaction terms between region and social adversity from Model II (from Table 5) revealing marked regional differences in the social prescribing gradient as indicated by IRRs for each social adversity level (reference group: region [at single parenthood and < 10 parental education] in Table 5). While the gradient was steeper in regions North and Middle (IRRs significantly below 1) compared with the Capital region, the gradient was very smooth in region South (IRRs all insignificant). Estimates for all other explanatory variables were identical in the 2 multivariable models.

DISCUSSION

Main Findings

In this Danish register-based cohort study, we aimed to explore whether regional differences in incident prescribing of attention-deficit hyperactivity disorder (ADHD)

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Table 3. Bivariate Kitagawa Decomposition[a] of National-to-Regional Differences in the Cumulative Incidence Proportion of Pediatric ADHD Prescribing (CIP): The Contribution of Difference Attributable to the Demographic Distribution of Social Indicators (the Sociodemographic Composition)[b]

			Region North					Region Middle				
Education, yrs	Cohabitation Status	National CIP, %[c]	CIP, %	CIP diff[d]	CIP attr[e]	Comp attr[f]	Comp attr%[g]	CIP, %	CIP diff	CIP attr	Comp attr	Comp attr%
<10	Single	1.053	1.904	0.037	0.043	−0.007		1.303	0.005	0.013	−0.007	
<10	Cohabiting	0.744	1.244	0.031	0.027	0.004		0.769	−0.001	0.001	−0.002	
10–12	Single	0.891	1.040	0.003	0.013	−0.009		0.852	−0.012	−0.003	−0.008	
10–12	Cohabiting	0.570	0.658	0.067	0.035	0.032		0.656	0.043	0.032	0.010	
13–15	Single	0.661	0.734	−0.003	0.003	−0.007		0.785	0.002	0.006	−0.004	
13–15	Cohabiting	0.397	0.431	0.011	0.010	0.001		0.438	0.020	0.012	0.008	
15+	Single	0.345	0.677	0.001	0.003	−0.003		0.385	−0.001	0.000	−0.001	
15+	Cohabiting	0.232	0.313	−0.002	0.006	−0.008		0.276	0.002	0.004	−0.002	
All	All	**0.554**	**0.697**	0.143	0.140	0.004	**3**	**0.612**	0.058	0.065	−0.007	**−11**

			Region South					Region Zealand				
Education, yrs	Cohabitation Status	National CIP, %	CIP, %	CIP Diff	CIP attr	Comp attr	Comp attr%	CIP, %	CIP Diff	CIP attr	Comp attr	Comp attr%
<10	Single	1.053	0.516	−0.028	−0.029	0.001		1.188	0.012	0.007	0.004	
<10	Cohabiting	0.744	0.566	−0.008	−0.009	0.001		0.770	0.003	0.001	0.002	
10–12	Single	0.891	0.581	−0.030	−0.027	−0.004		1.049	0.022	0.015	0.007	
10–12	Cohabiting	0.570	0.368	−0.064	−0.078	0.014		0.730	0.083	0.062	0.022	
13–15	Single	0.661	0.475	−0.011	−0.008	−0.003		0.805	0.007	0.007	0.000	
13–15	Cohabiting	0.397	0.254	−0.037	−0.042	0.005		0.551	0.035	0.042	−0.007	
15+	Single	0.345	0.265	−0.003	−0.001	−0.002		0.185	−0.003	−0.002	−0.001	
15+	Cohabiting	0.232	0.117	−0.015	−0.009	−0.006		0.230	−0.007	0.000	−0.006	
All	All	**0.554**	**0.359**	−0.195	−0.203	0.007	**−4**	**0.707**	0.153	0.133	0.020	**13**

[a]Kitagawa decomposition[21]: The full analysis is available in Supplementary Digital Content 2, http://links.lww.com/JDBP/A78.
[b]Social indicators: The combined effect of length of parental education and cohabitation status.
[c]CIP (%): Number of incident dispensed ADHD medications per 100 children during 2010–2011; Region Capital is not included due to insignificant CIP differences between this region and the national level.
[d]CIP diff: CIP differences between national and regional level (% points).
[e]CIP attr: CIP difference attributable to the national versus regional difference in CIP (% points).
[f]Comp attr: CIP difference attributable to national versus regional in the demographic composition of social indicators (% points).
[g]Comp attr%: Fraction (%) of the CIP difference between national and regional level attributable to differences in the demographic composition (100*comp attr/CIP diff).

medication for school-age children are explained by sociodemographic differences and/or differences in ADHD prescribing practice, especially for children facing social adversity (measured by low level of parental education and single parenthood).

Considerable regional ADHD prescribing differences were found, with the highest prescribing incidence in regions North and Zealand and the lowest in region South. The prescribing incidence decreased for all regions with increasing level of parental education for other explanatory variables, e.g. child's gender and age, parental age at child's birth, and ethnicity. While differences in the sociodemographic composition generally explained little of the regional variation in ADHD prescribing, the high ADHD prescribing in region Zealand was to a greater extent explained by the sociodemographic composition than in region North.

Instead, the analyses demonstrated large variations in prescribing practices for the most disadvantaged children, even after adjustment for other characteristics. For children of single parents with a low level of education, the incidence of ADHD prescribing was more than 4 times higher in region North compared with region South and twice as high compared with the Capital region. Adding to this, the gradient between the high ADHD prescribing incidence for disadvantaged children and the lower incidence for other children was steeper in region North and smoother in region South.

Strengths and Limitations

We consider it a strength that we followed an unselected nationwide cohort of school-age children in the Danish registries. The registries enabled us to link child and parent/caregiver data. The exclusion of children with previous psychiatric conditions should ensure that the cohort does not include children with an early onset neurodevelopmental disorder of more likely a genetic biological pathway, e.g. mental retardation and autism spectrum disorders. Assuming that pharmacological therapy for ADHD is initiated by specialists, we did not

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Table 4. Results of Region-Specific Poisson Regression Analyses[a]: Multivariable Analyses of Incident ADHD Medication Prescribing for School-Age Children Across the 5 Danish Regions

	Region											
	National		North		Middle		South		Capital		Zealand	
Explanatory Variables	**IRR**	**95% CI**	**IRR**	**95% CI**	**IRR**	**95% CI**	**IRR**	**95% CI**	**IRR**	**95% CI**	**IRR**	**95% CI**
Gender												
Boy	1.00	—	1.00	—	1.00	—	1.00	—	1.00	—	1.00	—
Girl	0.40	0.37–0.42	0.40	0.34–0.48	0.44	0.39–0.50	0.30	0.25–0.36	0.39	0.34–0.44	0.44	0.38–0.50
Child age group, yr												
5–8	1.00	—	1.00	—	1.00	—	1.00	—	1.00	—	1.00	—
9–12	0.93	0.86–1.00	0.88	0.73–1.07	0.91	0.79–1.06	0.83	0.69–0.99	1.07	0.94–1.23	0.88	0.75–1.04
13–17	0.77	0.72–0.83	0.57	0.47–0.70	1.03	0.90–1.18	0.57	0.48–0.69	0.80	0.70–0.92	0.77	0.66–0.90
Parental age at child's birth												
<20	1.00	—	1.00	—	1.00	—	1.00	—	1.00	—	1.00	—
20–34	0.70	0.65–0.75	0.60	0.50–0.73	0.75	0.64–0.87	0.56	0.47–0.68	0.73	0.62–0.85	0.83	0.70–0.98
35+	0.59	0.53–0.66	0.51	0.39–0.68	0.65	0.53–0.81	0.47	0.35–0.62	0.58	0.48–0.71	0.68	0.54–0.87
Parental psychiatric condition												
No	1.00	—	1.00	—	1.00	—	1.00	—	1.00	—	1.00	—
Yes	1.90	1.78–2.02	1.59	1.34–1.89	2.04	1.81–2.30	1.79	1.53–2.11	1.84	1.63–2.08	2.17	1.90–2.49
Parental country of birth												
Denmark	1.00	—	1.00	—	1.00	—	1.00	—	1.00	—	1.00	—
Western country	0.70	0.54–0.91	0.54	0.22–1.30	0.85	0.50–1.44	0.84	0.45–1.57	0.80	0.54–1.17	0.31	0.12–0.84
Nonwestern country	0.23	0.19–0.29	0.13	0.04–0.39	0.32	0.21–0.50	0.16	0.07–0.37	0.33	0.24–0.45	0.02	0.00–0.15
Parents' length of education, yr												
<10	1.00	—	1.00	—	1.00	—	1.00	—	1.00	—	1.00	—
10–12	0.85	0.78–0.93	0.59	0.47–0.73	0.81	0.68–0.97	1.02	0.81–1.29	0.93	0.79–1.11	0.99	0.81–1.20
13–15	0.63	0.57–0.70	0.41	0.32–0.53	0.61	0.50–0.74	0.78	0.60–1.02	0.65	0.54–0.79	0.80	0.64–1.01
15+	0.38	0.32–0.44	0.41	0.25–0.69	0.43	0.31–0.59	0.42	0.22–0.79	0.41	0.33–0.51	0.39	0.24–0.64
Parental cohabitation status												
Single	1.00	—	1.00	—	1.00	—	1.00	—	1.00	—	1.00	—
Cohabiting	0.67	0.63–0.72	0.59	0.48–0.71	0.67	0.59–0.78	0.66	0.55–0.79	0.65	0.57–0.73	0.74	0.63–0.86

[a]The Poisson parameters of all explanatory variables (except parents' education and cohabitation status) are directly standardized to the demographic distribution of social adversity indicators at the national level.
CI, confidence interval; IRR, incidence rate ratios.

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Table 5. Results of the Unified Poisson Regression Analyses[a]: Multivariable Analyses of Regional Variation in Incident ADHD Medication Prescribing for School-Age Danish Children

	Model I[b]		Model II[c]	
ıatory Variables	IRR		IRR	95% CI
Gender				
Boy	1.00	—	1.00	—
Girl	0.40	0.37–0.42	0.40	0.37–0.42
Child age group, yr				
5–8	1.00	—	1.00	—
9–12	0.93	0.86–1.00	0.93	0.86–1.00
13–17	0.77	0.72–0.83	0.77	0.72–0.83
Parental age at child's birth				
<20	1.00	—	1.00	—
20–34	0.70	0.65–0.76	0.70	0.65–0.76
35+	0.58	0.53–0.65	0.58	0.53–0.65
Parental psychiatric condition				
No	1.00	—	1.00	—
Yes	1.91	1.80–2.03	1.91	1.80–2.03
Parental country of birth				
Denmark	1.00	—	1.00	—
Western country	0.71	0.55–0.92	0.71	0.55–0.92
Non-Western country	0.24	0.19–0.30	0.24	0.19–0.30
Region				
Capital	1.00	—	1.00	—
North	1.19	1.08–1.32	2.00	1.51–2.66
Middle	1.07	0.99–1.16	1.30	1.01–1.68
South	0.60	0.54–0.66	0.47	0.34–0.65
Zealand	1.17	1.08–1.28	1.09	0.83–1.43
Social adversity level[d]			For the interaction, Region*Social Adversity, see Table 6	
0: <10: Single	1.00	—		
1: <10: Cohabiting	0.81	0.70–0.94		
2: 10–12: Single	0.95	0.84–1.07		
3: 10–12: Cohabiting	0.61	0.55–0.68		
4: 13–15: Single	0.74	0.64–0.87		
5: 13–15: Cohabiting	0.45	0.40–0.51		
6: 15+: Single	0.47	0.35–0.62		
7: 15+: Cohabiting	0.28	0.24–0.33		

[a]The Poisson parameters of all explanatory variables (except education and cohabitation status) are directly standardized to the national distribution of social indicators.
[b]Model I: Regression analyses without inclusion of interaction terms. Region reflects the regional difference adjusted for the *common* social adversity prescribing gradient.
[c]Model II: Inclusion of interaction between region and the combined social adversity indicator (1–7): Region: Reflects difference at *social adversity level 0* for each region, which is the reference group for the region-specific interactions in Table 6.
[d]Social adversity level: Combination of parental education (years) and cohabitation status.
CI, confidence interval; IRR, incidence rate ratios.

explore the extent to which children initiating ADHD medication were diagnosed with ADHD during the observation period. Hence, the potential influence of social adversity on being diagnosed with ADHD in childhood was not explored in this study. The main strength of the study lies in our methodology to tease out the effect of regional variation in sociodemography and possible regional difference in ADHD prescribing practice regarding children who face social adversity. While the Kitagawa method[28] is a straightforward bivariate method to decompose these 2 nested effects, our method to eliminate the difference in demographic composition in a standardized multivariable Poisson regression model is considered a strength, because neither the stratified multivariable Poisson model nor a multilevel Poisson model would do the job of exploring the differences in

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Table 6. Interaction Terms Between Region and Social Adversity Level from the Unified Poisson Regression Analyses (Table 5, Model II)

		Interaction Term for Model II: Region*Social Adversity Level[a]									
		Capital		North		Middle		South		Zealand	
Social Adversity Level[b]		IRR	95% CI	IRR	95% CI	IRR	95% CI	IRR	95% CI	IRR	95% CI
0: <10:	Single	1.00	—	1.00	—	1.00	—	1.00	—	1.00	—
1: <10:	Cohabiting	0.95	0.71–1.27	0.62	0.44–0.87	0.65	0.48–0.88	1.21	0.83–1.77	0.73	0.51–1.03
2: 10–12:	Single	1.13	0.91–1.40	0.59	0.43–0.83	0.72	0.56–0.94	1.38	0.98–1.94	1.02	0.77–1.33
3: 10–12:	Cohabiting	0.64	0.52–0.79	0.36	0.28–0.46	0.55	0.45–0.68	0.84	0.62–1.13	0.74	0.58–0.93
4: 13–15:	Single	0.72	0.55–0.93	0.44	0.27–0.72	0.74	0.54–1.01	1.23	0.80–1.89	0.85	0.60–1.21
5: 13–15:	Cohabiting	0.48	0.38–0.60	0.25	0.19–0.34	0.38	0.30–0.48	0.61	0.45–0.84	0.61	0.47–0.79
6: 15+:	Single	0.45	0.31–0.66	0.72	0.26–1.98	0.48	0.22–1.03	1.37	0.43–4.37	0.30	0.07–1.22
7: 15+:	Cohabiting	0.30	0.23–0.38	0.23	0.13–0.40	0.27	0.19–0.39	0.28	0.13–0.60	0.31	0.18–0.53

[a]Interaction terms between Region and Social Adversity (Region*Social adversity) from the unified multivariable Poison analysis in Table 5, Model II, showing the reference category, i.e. IRRs for children at the lowest social adversity level (0) for each region compared with the Capital. This table displays the interaction term between each region and all remaining social adversity levels (1–7), i.e. IRRs (1–7) compared with the lowest level (0) for each region shown in Table 5.
[b]Social adversity level: Combination of parental education (years) and cohabitation status.
CI, confidence interval; IRR, incidence rate ratio.

the socially patterned prescribing practice. In contrast to the standard method of performing direct standardization, we based our calculation on the distribution of risk time rather than the distribution of individuals. Although this standardization method constitutes a potential limitation because time to first ADHD prescribing (risk time) will not exactly correspond to the distribution of persons, we argue that this error will be negligible as long as the event is rare. The unified model demonstrated that the standardization merely affected estimates related to the social adversity variables, indicating that the standardization did not distort data. However, the multivariable extensions of the Kitagawa method[29] could also have been applied for continuity.

The study has several potential limitations regarding the operationalization of variables. To keep it simple, we applied 2 indicators for the degree of social adversity: parental education and cohabitation status. We did not include income because educational level and income are associated in Denmark, and because parental educational level has been shown to be a much stronger predictor for ADHD medication in childhood.[14,15] Nevertheless, financial constraints may reinforce the negative consequence of low parental educational level and single parenthood on children's development and social competences. On the other hand, low income may prevent the purchase of prescribed prescriptions (information on "primary noncompliance" is not available in the Danish registries).

We defined parent(s) or caregiver(s) corresponding to register information on actual household, which may be regarded as a limitation because the actual caregiver(s) may neither correspond to the biological parent(s) nor represent the most important caregiver in the child's life. However, we do not believe that a more complex definition would have improved the validity of our study. Focusing on familial social adversity, we excluded children not cohabitating with their parents, e.g. children living in institutions. Hence, the prescribing of ADHD medication for this potentially most vulnerable group of children needs to be explored in future studies. In line with a recent Swedish study,[14] we included parents' previous psychiatric condition as a potential confounder. However, we applied both information on in-hospital psychiatric diagnoses and dispensing of medications for psychiatric conditions to include psychiatric problems handled in primary care. As our data package from Statistics Denmark does not contain information on prescribed antipsychotic medicines, we may have misclassified adults using antipsychotic medication. Therefore, we may have underestimated the impact of parents' psychiatric conditions, but it is unlikely that this presumably nondifferential misclassification bias has distorted our estimates significantly.

Implications and Comparisons with Other Studies

While other studies have demonstrated that social adversity predicts prescribing of ADHD medication,[14,15] our study has demonstrated regional variations in ADHD prescribing practice for children from equally disadvantaged families. These regional variations were observed despite the fact that national ADHD guidelines exist, emphasizing that ADHD therapy in children is a specialist task.[25] The Danish National guidelines[25,30] follow the ICD-10 diagnostic criteria[24] recommending a standardized assessment of core symptoms and evaluation of impairment, both based on observations from parents and teachers. The guidelines suggest psychosocial interventions, parental training, and psychoeducation for mild and moderate cases, whereas pharmacological treatment is recommended as the main treatment for severe cases. The nonpharmacological treatments (mainly offered by local social and educational services) are free of charge for children with an ADHD diagnosis. Hence, the regional ADHD prescribing

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variation is unlikely to reflect formal differences in the affordability of these services.

The large differences between regions North and South in ADHD prescribing for socially disadvantaged children may indicate different interpretations of poor-performing school children, perhaps reflected by differences regarding the decision to initiate pharmacological therapy as well as the diagnostic assessment. The much smoother social prescribing gradient in region South (with an overall low-prescribing rate) compared with region North (with an overall high-prescribing rate) may further indicate that only part of the observed social gradient in ADHD is explained by genetic or biological pathways, and the rest by cultural issues. Our finding that the incidence of ADHD prescribing decreases with increasing paternal education over the whole range of more biological explanatory variables (e.g., parental age at child's birth and ethnic background) also indicates that culturally embedded factors play a key role in the interpretation and handling of children with behaviors compatible with ADHD symptoms.

In contrast to our findings, a US study has demonstrated that children from low-income families are less likely to be prescribed or purchase ADHD medication compared with children from high-income families, although these children are more likely to meet criteria for ADHD.[31] This discrepancy may reflect both differences in health care insurance systems and different attitudes regarding the use of psychotropic medication for children.[32] In the United States, low-income families may be less likely than high-income families to fill ADHD prescriptions for their children due to financial constraints,[31] whereas the universal Danish health care system ensures high reimbursement for prescription medicines to children. Different attitudes about ADHD medication in children[19] among socially advantaged parents in the United States and Denmark may also exist, which would explain some of this opposing social ADHD medication gradient.

In line with other studies,[11,33] we found a higher ADHD medication rate in boys than in girls, potentially not merely reflecting gender differences in the prevalence of ADHD but also gender-related referral bias.[34] We demonstrated further that this gender difference diminished with age, potentially because younger school girls tend to have more sedentary and dutiful behaviors well-suited to the classroom, a pattern that may reverse during the teenage years. These gender-age differences need to be explored in future studies, comparing, for example, preschoolers with school-age children.

Also in accordance with previous studies,[15,35] our study demonstrated marked ethnic differences regarding ADHD prescribing. Although ethnic/racial differences may be explained by genetic biological pathways, the lower use of ADHD medication may also reflect cultural differences in the interpretation of behavioral problems and help-seeking behavior, as well as attitudes toward psychotropic medication.[35,36] For both parents and professionals, certain behaviors may be regarded as antisocial in children from the majority groups, whereas the same behaviors may be regarded as normal or even typical in children from minority groups. This culture-embedded interpretation of behaviors most likely also applies for teachers, psychologists, and parents, which may result in poor-performing children being sent to the health care system.[32,37] This situation may partly be a consequence of increased pressure on school performance[38] combined with a demand for diagnoses if extra teaching resources are needed.

Our finding that regional variation in ADHD prescribing partially mirrors differences in prescribing practice for socially disadvantaged children may be a consequence of several factors. It is likely that the regional ADHD prescribing variation in Denmark reflects the decentralized responsibility for both primary school education and child and adolescent psychiatric centers. This may lead to regional differences regarding the prioritizing of pedagogical support to children not matching standard schooling programs, health care referrals for ADHD symptoms, and differences regarding symptom interpretation combined with physicians' different attitudes toward medicating children with ADHD-like behaviors, as described by Kovshoff et al.[27]

The fact that the ADHD diagnosis is based on significant functional impairment in terms of social, educational, or occupational competences[3] may lead to a context-bound diagnostic practice,[39,40] because the interpretation of behavioral competences will inevitably be culture-embedded in conceptions of normality and disease.[5,37] School systems with increasing focus on complex academic skills may reinforce the functional challenges among socially disadvantaged children who may have relatively little parental support, academic aspiration, and low-social mobility in their local milieu.[5] This situation may increase the risk of socially disadvantaged children being diagnosed with ADHD and subsequently prescribed ADHD medication. Thus, the seemingly context-bound ADHD prescribing practice for socially disadvantaged children found in our study may cover a combination of context-bound diagnostic and prescribing practices. Hence, additional research is needed to explore potential regional variation in both diagnostic thresholds and prescribing practices, particularly regarding socially disadvantaged children.

Although the actual interpretation and handling of specific children is most likely interplay between the professional attitude toward medication and external pressure from teachers or parents,[27] the observed regional prescribing variation may indicate that the attitudes and practices among Danish regional child psychiatrists and psychologist shape regional prescribing practice. This phenomenon is most likely not unique to Danish society.[5,7,37,39,40] In contrast to Russell et al,[7] our study indicates a clinical bias toward prescribing ADHD medication for children facing social adversity, with the potential result of overprescribing symptom-reducing

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psychotropic medication for vulnerable children who may instead need psychosocial support and acceptance.

CONCLUSIONS

While a minor part of the regional variation in incident prescribing of attention-deficit hyperactivity disorder (ADHD) medication for children was explained by differences in sociodemographic composition, large variations were observed in prescribing practice with both higher incidence of ADHD prescribing for socially disadvantaged children and a steeper social prescribing gradient in regions with higher prescribing incidence. The regional variations were observed despite tax-financed access to non-pharmacological options and national guidelines on ADHD diagnostics and therapeutic options. Hence, our findings indicate that local cultures shape the interpretation and handling of children with ADHD-like behaviors, particularly as regards children facing social adversity.

Approval of Data Access

Access to data was provided and secured through collaboration between the University of Copenhagen and Statistics Denmark. Approval was obtained from the Danish Data Protection Agency through Statistics Denmark. No person identifiers were provided to the researchers, and purely registry-based studies do not require ethical approval according to Danish law.[20]

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