

Infant-onset eczema in relation to mental health problems at age 10 years: Results from a prospective birth cohort study (German Infant Nutrition Intervention plus)

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Background: Cross-sectional studies suggest an association between eczema and mental health problems, but the temporal relationship is unclear.

Objective: To assess the association between infant-onset eczema and mental health problems in a prospective study.

Methods: Between 1995 and 1998, a birth cohort study was recruited and followed until age 10 years. Physician-diagnosed eczema, comorbidities, and a broad set of environmental exposures were assessed at age 1, 2, 3, 4, 6, and 10 years. First, we investigated the association between infant-onset eczema (age 1-2 years) and mental health problems at age 10 years according to the Strengths and Difficulties Questionnaire. Second, we analyzed the likelihood of mental health problems at age 10 years in relation to the course of eczema.

Results: A total of 2916 infants were eligible for analysis.

Compared with participants never diagnosed as having eczema, children with infant-onset eczema had a significantly increased

risk for possible/probable mental health problems (Strengths and Difficulties Questionnaire total score) at age 10 years (odds ratio, 1.49; 95% CI, 1.13-1.96) and for emotional symptoms (odds ratio, 1.62; 95% CI, 1.25-2.09). Eczema limited to infancy predicted a significantly higher risk for conduct problems at age 10 years. The strength of the association between eczema and emotional problems at age 10 years increased with increasing eczema persistence.

Conclusion: Infants with eczema are at increased risk for mental health problems at age 10 years. Even if cleared afterward, eczema at age 1 to 2 years may cause persistent emotional and behavioral difficulties. (*J Allergy Clin Immunol* 2010;125:404-10.)

Key words: Eczema, cohort study, depression, emotional problems, hyperactivity, infant, risk, Strengths and Difficulties Questionnaire

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Eczema is one of the most prevalent chronic conditions in children and adolescents. The incidence of eczema peaks within the first 2 years of life and decreases thereafter.¹ Approximately 60% of patients with eczema in early childhood are free of symptoms in adolescence.² It is well established that children with eczema are at increased risk for allergic rhinitis and/or allergic asthma: in the subset of patients with atopic eczema (eczema with concomitant allergic sensitization), the itchy lesions often represent the beginning of the atopic march.³

Recent investigations indicate that comorbidities of eczema are not limited to allergic conditions, but that children and adolescents with eczema are diagnosed as having mental health problems such as attention-deficit/hyperactivity disorder (ADHD) significantly more frequently than children without a history of eczema.^{4,5} Stressful life events like divorce of parents have been shown to increase significantly the incidence of eczema in children.^{6,7} Adults with prevalent eczema have been shown to be at increased risk for a broad set of psychiatric conditions including depression, stress-related disorders, and behavior disorders.^{8,9} A significant limitation of these recently published studies on the association between eczema and psychosomatic/psychiatric difficulties is their cross-sectional design, so that the temporal relationship between eczema and mental health problems is still unclear.^{4,5,8}

We analyzed data from a large prospective birth cohort study with a follow-up period of 10 years to investigate the temporal relationship between eczema and psychopathological symptoms. We hypothesized that infants with eczema are at increased risk of

Abbreviations used

ADHD: Attention-deficit/hyperactivity disorder
GINI: German Infant Nutrition Intervention
OR: Odds ratio
SDQ: Strengths and Difficulties Questionnaire

mental health problems including emotional problems, conduct problems, and hyperactivity/inattention at age 10 years compared with children without a history of eczema.

METHODS

Study design

In the German Infant Nutrition Intervention plus (GINIplus) study, 5991 children born between 1995 and 1998 were recruited in 2 German cities (Munich and Wesel). Details of the study design have been described elsewhere.¹⁰⁻¹²

The parents of 2252 newborns with a positive family history of allergic disease (intervention group) agreed to participate in a randomized controlled trial to compare the effect of hydrolyzed formulas versus conventional cow's milk formula on the development of allergic diseases. Mothers were encouraged to breast-feed for at least 4 months and were advised to feed the randomly allocated formula in case of insufficient breast-feeding. It was recommended not to introduce solid foods during the first 4 months of life and to introduce only 1 new food per week after that. All infants with a negative family history of allergic disease and infants with a positive family history whose parents did not wish to take part in the trial ($n = 3739$) were allocated to the nonintervention group. This group did not receive any dietary recommendation or intervention. Children from both groups were followed up at 1, 2, 3, 4, 6, and 10 years of age. Questionnaires were administered by mail a few weeks before the child's birthday, and there was a maximum time window of 1 year for the reception of the completed questionnaires for the follow-up conducted at age of 4, 6, and 10 years. For the follow-ups during the first 3 years of life, a tighter time window of less than 6 months was applied.

Exposure and confounding variables

Questionnaires were administered at baseline and after 1, 2, 3, 4, 6, and 10 years.

Information on the main exposure ("Doctor-diagnosed eczema in first and/or second year of life") was taken from the 1-year and 2-year questionnaires. Parents were asked, "Did a physician diagnose any of the following diseases during the 1st/2nd year of life: ... allergic or atopic eczema/dermatitis?" For those children who reported having been diagnosed with eczema for the first time after their first 2 years of life, we created a variable "doctor-diagnosed eczema reported between 3 and 10 years" and also a variable "ever doctor-diagnosed eczema." Children who reported physician diagnosed eczema in infancy and also at age 10 years were classified as having "infant-onset eczema persisting until age 10 years."

The set of confounding variables was chosen based on known confounding factors. Information on sex (male/female), living area (Munich/Wesel), participation/nonparticipation in the German Infant Nutrition Intervention (GINI) trial (reflecting a positive vs a negative family history of atopy), and parental education (less than 10 years of schooling, 10 years of schooling, more than 10 years of schooling) was taken from the baseline questionnaire. Information on exclusive breast-feeding for at least 4 months was obtained from the 1-year questionnaire. Information whether the child was living with a single parent at age 10 years was obtained from the 10-year questionnaire. For the variables "asthma ever" and "rhinitis ever," information from birth until the 10-year questionnaire was combined to create the variables.

Outcome

At the 10-year follow-up examination, the German version of the Strengths and Difficulties Questionnaire (SDQ) was completed by the parents.¹³ The SDQ

is a screening questionnaire used to detect behavioral strengths and difficulties of children 3 to 16 years old. Each of its 5 subscales consists of 5 items with 3 response options ("not true," "somewhat true," "certainly true"). The SDQ total difficulties scale is composed of the subscales "emotional problems," "conduct problems," "hyperactivity/inattention," and "peer problems," but not the "pro-social behavior" domain that assesses positive social behavior.

The cutoff points of the German validation^{13,14} were chosen to classify about 10% of children as "borderline" and 10% as "abnormal." According to these cutoff points, the respective symptom domains (subscales) and the total score are classified as "unlikely," "possible," or "probable." These 3 categories were used for descriptive analyses in this article.

Statistical analysis

Counts and percentages were calculated for each of the confounding variables as well as for the 3 categories of the SDQ total and the 5 SDQ domains and tabulated against the different eczema categories (eczema in first/second year of life; first manifestation of eczema at age 3-10 years; eczema ever; eczema never). The χ^2 test was used to compare the characteristics of participants with complete follow-up versus participants lost to follow-up and of children with infant-onset eczema versus children without eczema.

To assess internal validity of the SDQ in our sample, we calculated the Cronbach α for the SDQ total score and each SDQ domain.

Multivariable logistic regression models were then fitted by using a dichotomized outcome "possible/probable" versus "unlikely" (for the total score and each subscale). The aforementioned variables were included in the models as potential confounders.

All analyses were carried out by using STATA, version 10 (STATA Corp, College Station, Tex). The study protocol was approved by the local ethics committees (Bavarian General Medical Council, Medical Council of North Rhine Westphalia), and written consent was obtained from all participating families.

RESULTS

Study population and follow-up

Fig 1 shows the flow of the study population from screening of newborns through to the 10-year follow-up. The original cohort included 5991 newborns, 2252 and 3739 of whom belonged to the intervention group and nonintervention group, respectively. A total of 4671 children participated in the 1-year assessment, and 2985 children were followed up at age 10 years. The following analyses are based on 2916 children with complete follow-up information until the age of 10 years and without missing information on the exposure of interest (ie, eczema in first 2 years of life) or on the outcome of interest (ie, SDQ at age 10 years; Fig 1).

The prevalence of eczema at age 1 year did not differ between children with complete ($n = 2916$; eczema prevalence, 10%) and incomplete follow-up ($n = 1755$; eczema prevalence, 10%; $P = .72$). The dropout rate was higher for boys ($P = .03$) and for children of parents with a low level of school education ($P < .001$).

Participant characteristics

From the 2916 children analyzed, 17% had infant-onset eczema, 10% had eczema with manifestation after age 2 years, and 73% were never diagnosed as having eczema until age 10 years. Baseline characteristics of the study population and potential confounding factors are given in Table I.

Children with infant-onset eczema were less likely to be girls than children without eczema ($P = .004$). Children with infant-onset eczema and children without eczema did not differ significantly with regard to parental education ($P = .88$), parental divorce/separation from 1 parent ($P = .10$), or breast-feeding status ($P = .58$).

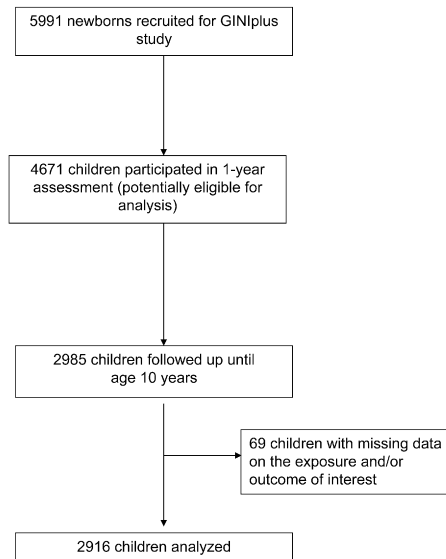


FIG 1. Flow chart of study population. *GINIplus*, German Infant Nutrition Intervention plus.

Allergic rhinitis and allergic asthma were more prevalent in children with infant-onset eczema compared with children without eczema ($P < .001$ for both comparisons; [Table I](#))

Internal consistency analysis

In our sample, the internal consistency of SDQ total score and each SDQ domain was adequate, with Cronbach α values almost identical to those of the German SDQ validation study (SDQ total score, $\alpha = 0.80$; SDQ domain emotional problems, $\alpha = 0.67$; SDQ domain conduct problems, $\alpha = 0.51$; SDQ domain hyperactivity/inattention, $\alpha = 0.80$; SDQ domain peer problems, $\alpha = 0.62$).

Relationship of infant-onset eczema and psychopathologies at age 10 years

As displayed in [Table II](#), a higher proportion of children with infant-onset eczema had possible or probable mental health problems according to the SDQ total score at 10-year follow-up ($P < .001$). Among the SDQ domains, emotional symptoms were strongly associated with infant-onset eczema ($P < .001$). Conduct problems were also more prevalent in children with infant-onset eczema than in children without eczema ($P = .03$). Children with infant-onset eczema tended to be classified as hyperactive/inattentive more often than children without eczema, but this association was not statistically significant ($P = .12$). Peer problems were not related to eczema ($P = .85$).

[Table III](#) summarizes the results of the logistic regression modeling. The odds ratio (OR) for the crude association between infant-onset eczema and possible/probable psychopathology (SDQ total score) at age 10 years was found to be 1.75 (95% CI, 1.35-2.27). Adjustment for potential environmental and sociodemographic confounders and for comorbid allergic rhinitis and allergic asthma slightly decreased the strength of the association (fully adjusted model: OR, 1.49; 95% CI, 1.13-1.96).

A moderately strong association was also observed between emotional symptoms and infant-onset eczema as well as eczema ever and eczema manifesting after age 2 years. In the crude

(univariate) analysis, children with infant-onset eczema were at significantly increased risk for conduct problems at age 10 years, but this association was not statistically significant in the fully adjusted model. Hyperactivity/inattention was also related to infant-onset eczema in the crude analysis, but this association was explained in part by confounding by sociodemographic factors (mainly sex) and atopic comorbidity.

Subgroup analyses

We discriminated infant-only eczema (eczema cleared after age 2 years) and infant-onset eczema persisting after age 2 years. The latter group was subdivided into children with persisting infant-onset eczema until age 10 years and in children with remission of eczema between the ages of 2 and 10 years. All 3 subgroups of children with infant-onset eczema were at a significantly higher risk for psychopathological symptoms (SDQ total score) than children without eczema ([Table IV](#)). This association was strongest for children with infant-onset eczema persisting until age 10 years. Children with eczema only in infancy had a significantly higher risk for emotional and conduct problems and tended to have increased levels of hyperactivity/inattention at age 10 years. Emotional problems were even more prevalent in those children with persistence of eczema beyond infancy. Hyperactivity/inattention and conduct problems were not significantly associated when eczema persisted beyond infancy.

DISCUSSION

Main findings

Our study indicates that children with physician-diagnosed eczema within their first 2 years of life are at statistically significantly increased risk for mental health problems at age 10 years compared with children without eczema. They show more emotional difficulties and conduct problems. Even if cleared after the first 2 years of life, infant eczema appears to be independently associated with emotional symptoms, conduct problems, and possibly also hyperactivity/inattention at age 10 years. This finding suggests that early eczema symptoms have long-lasting adverse effects on the development and mental health of children and adolescents. According to our findings, not only children with infant-onset eczema but also children with eczema manifestation after age 2 years are at increased risk for mental health problems at age 10 years.

Skin lesions and concurrent symptoms cause problems in various dimensions of health-related quality of life such as daily activities, leisure, school/work, and personal relationships in many patients.^{15,16} Before this prospective study, we investigated the association between eczema and mental health in 3 large population-based cross-sectional samples. Secondary data from routine outpatient practice indicated a significant association between eczema and ADHD in children and adolescents that was independent from sociodemographic factors and atopic comorbidity, but probably related to eczema severity.⁴ In a random sample from the German population, children age 3 to 17 years with a history of eczema were more likely to have ever been diagnosed with ADHD by a physician compared with children without eczema.⁵ In a matched-pairs sample of 3769 adults with eczema and controls without eczema, we observed a significant association between eczema and major psychiatric disorders such as

TABLE I. Characteristics of the cohort under study, stratified by the age of the onset of eczema (n = 2916)

Characteristic	Onset of eczema							
	Eczema in first/ second year of life (n = 484)		Eczema manifesta- tion at age 3-10 y (n = 296)		Eczema ever (n = 780)		Never eczema (n = 2136)	
	No.	Percent	No.	Percent	No.	Percent	No.	Percent
Female sex	209	43	163	55	372	47	1078	51
Living area								
Munich	279	58	171	58	450	58	1082	51
Wesel	205	43	125	42	330	42	1054	49
Intervention group*								
Intervention	241	50	159	54	400	51	1360	64
Nonintervention	243	50	137	46	380	49	776	36
Social status (parental education)								
<10 y of schooling	36	8	23	8	59	8	168	8
10 y of schooling	146	30	73	25	219	28	622	29
>10 y of schooling	300	62	199	68	499	64	1332	63
Single parent (at age 10 y)	59	12	37	13	96	13	206	10
Exclusive breast-feeding for ≥ 4 mo	277	57	175	59	452	58	1193	56
Allergic rhinitis (ever, physician-diagnosed)	126	26	60	20	186	24	199	9
Allergic asthma (ever, physician-diagnosed)	61	13	36	12	97	12	107	5

*Referring to GINI intervention study vs GINI observational study.

TABLE II. Mental health problems at age 10 years according to SDQ

Characteristic	Onset of eczema							
	Eczema in first/sec- ond year of life (n = 484)		Eczema manifesta- tion at age 3-10 y (n = 296)		AE total (n = 780)		No eczema (n = 2136)	
	No.	Percent	No.	Percent	No.	Percent	No.	Percent
Mental health problems (SDQ total)								
Unlikely	369	80	237	82	606	81	1802	87
Possible	41	9	19	7	60	8	138	7
Probable	54	12	33	11	87	1	127	6
Emotional symptoms								
Unlikely	353	76	219	76	572	76	1757	85
Possible	42	9	25	9	67	9	141	7
Probable	69	15	45	16	114	15	169	8
Conduct problems								
Unlikely	397	86	249	86	646	86	1852	90
Possible	40	9	21	7	61	8	144	7
Probable	27	6	19	7	46	6	72	4
Hyperactivity/inattention								
Unlikely	391	84	245	85	636	85	1815	88
Possible	29	6	15	5	44	6	101	5
Probable	44	10	29	10	73	10	151	7
Peer problems								
Unlikely	422	91	266	92	688	91	1896	92
Possible	21	4	14	5	35	5	88	4
Probable	21	4	9	3	30	4	83	4

depression, stress-related disorders, and behavior disorders.⁸ Our study extends previous research because it is the first prospective analysis of the association between eczema and mental health problems in a large sample of children.

Possible explanations

On the basis of cross-sectional data from the US National Survey of Children's Health, it has been suggested that children

with asthma are at high risk of developmental, emotional, and behavioral problems.¹⁷ The Early Treatment of the Atopic Child (ETAC) study suggested that behavior problems are not secondary psychological reactions to asthma but may precede asthma onset in young children.¹⁸ However, eczema has previously not been considered as a potential confounder and/or explanatory (exposure) variable.^{17,18} Because eczema is prevalent in many children with incident allergic asthma,^{3,19} the presence of eczema appears to contribute to or may be an underlying cause for the

TABLE III. OR estimates for SDQ probable/possible vs unlikely (total and domains) in relation to different clinical courses of eczema*

Exposure variable Reference (never eczema)	Univariate (unadjusted) analysis		Multivariate analysis (adjusted for environmental and sociodemographic factors)†		Multivariate analysis (adjusted for environmental factors, sociodemographics, and atopic comorbidity)‡	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
SDQ total						
Eczema in infancy	1.75 (1.35-2.27)	<.001	1.61 (1.23-2.11)	<.001	1.49 (1.13-1.96)	.005
Eczema at age 3-10 y	1.49 (1.08-2.07)	.02	1.50 (1.07-2.10)	.02	1.43 (1.01-2.00)	.04
Eczema ever	1.65 (1.32-2.05)	<.001	1.57 (1.25-1.97)	<.001	1.48 (1.17-1.87)	.001
Emotional symptoms						
Eczema in infancy	1.78 (1.39-2.28)	<.001	1.71 (1.33-2.21)	<.001	1.62 (1.25-2.09)	<.001
Eczema at age 3-10 y	1.81 (1.34-2.43)	<.001	1.80 (1.33-2.43)	<.001	1.74 (1.29-2.35)	<.001
Eczema ever	1.79 (1.46-2.20)	<.001	1.75 (1.41-2.16)	<.001	1.69 (1.36-2.10)	<.001
Conduct problems						
Eczema in infancy	1.45 (1.08-1.94)	.01	1.34 (0.99-1.80)	.06	1.31 (0.97-1.78)	.08
Eczema at age 3-10 y	1.38 (0.96-1.97)	.08	1.34 (0.93-1.95)	.12	1.33 (0.91-1.93)	.14
Eczema ever	1.42 (1.11-1.82)	.01	1.34 (1.04-1.73)	.03	1.32 (1.02-1.71)	.04
Hyperactivity/inattention						
Eczema in infancy	1.34 (1.01-1.78)	.04	1.21 (0.90-1.63)	.21	1.19 (0.88-1.61)	.26
Eczema at age 3-10 y	1.29 (0.91-1.83)	.15	1.38 (0.96-1.97)	.08	1.37 (0.95-1.96)	.09
Eczema ever	1.32 (1.05-1.68)	.02	1.27 (0.99-1.63)	.06	1.25 (0.97-1.61)	.08
Peer problems						
Eczema in infancy	1.10 (0.77-1.57)	.59	1.02 (0.71-1.47)	.90	0.90 (0.62-1.30)	.56
Eczema at age 3-10 y	0.96 (0.61-1.51)	.86	0.92 (0.58-1.46)	.72	0.82 (0.51-1.31)	.40
Eczema ever	1.05 (0.78-1.41)	.76	0.98 (0.73-1.34)	.92	0.87 (0.63-1.19)	.37

*Cutoff between "unlikely" and "possible" as the threshold for identification of psychopathologies (Foreman 2008).³¹

†Adjusted for sex, location, interventional arm, parental education, breast-feeding, and single parent.

‡Adjusted for sex, location, interventional arm, parental education, breast-feeding, single parent, allergic asthma (ever, physician-diagnosed), and allergic rhinitis (ever, physician-diagnosed).

observed behavior problems that precede asthma in young atopic children.¹⁸ Therefore, primary prevention of eczema may have a role in preventing mental health difficulties in children. Long-term follow-up data of the GINI trial have recently been published²⁰ showing a long-term preventive effect of hydrolyzed infant formulas (vs conventional cow milk's formula) on eczema until 6 years of age. Using hydrolyzed formulas might thus also be 1 avenue for the prevention of mental health difficulties in children.

In this prospective study, adjustment for allergic asthma and allergic rhinitis had no relevant influence on the association between eczema in early childhood and subsequent psychopathological symptoms. With the duration of eczema persistence in childhood, the association between eczema and conduct problems and hyperactivity/inattention symptoms seems to diminish, whereas emotional problems become more and more prominent. In addition, persistent eczema until age 10 years may also lead to peer problems in a subgroup of children.

However, even though the association between eczema and psychiatric disorders and psychopathological symptom domains is now well established and the study at hand suggests that eczema precedes and modifies mental health, the underlying mechanisms are yet unresolved. One may also speculate that psycho-neuro-endocrine factors could be an underlying cause of both eczema and mental health problems. In light of studies indicating dysfunctional responsiveness of the hypothalamus-pituitary adrenal axis with consecutive inappropriate regulation of the immune system under stressful conditions in patients with eczema and also in various mental health disorders, this hypothesis deserves further investigation.^{21,22} Our finding that children

whose eczema resolves by age 2 years have mental health risks at age 10 years may possibly be explained by an interruption of normal attachment between mother and child sometimes accompanying serious eczema.

We previously hypothesized that eczema-associated problems like sleep disturbance or itchy rash may cause, induce, or exacerbate ADHD symptoms.^{4,5} Interestingly, the strength of the association between eczema and emotional problems at age 10 years increased with increasing eczema persistence. Still, disposition to affective dysregulation in children with infant eczema may as well be the causative risk factor for persistence of eczema. The differential pattern of psychopathology in children with persisting compared with nonpersisting eczema may also be indicative of distinct underlying neurobiological underpinnings because of etiological heterogeneity.

Study strengths and limitations

A major strength of our study is the prospective design allowing us to capture a detailed and unbiased picture of the course of eczema in almost 3000 newborns until age 10 years.

To our knowledge, this is the first study that used the SDQ to assess psychopathological strengths and difficulties in children with eczema. The SDQ addresses a well balanced number of negative and positive behavioral attributes with domains and items closely corresponding to the major categories of current psychiatric classification systems.^{23,24} Children of parents with low socioeconomic status are more likely to have mental health problems but may be less likely to be diagnosed and treated as having mental health problems because of limited access to health

TABLE IV. OR estimates for SDQ probable/possible vs unlikely (total and domains) in relation to different levels of eczema persistence*

Exposure variable	Univariate (unadjusted) analysis		Multivariate analysis (fully adjusted model)†	
	OR (95% CI)	P value	OR (95% CI)	P value
SDQ (total score)				
Eczema in infancy (reference: never; n = 2136)				
Only in infancy (age 1-2 y; n = 208)	1.76 (1.22-2.55)	.002	1.57 (1.08-2.30)	.02
Eczema until age 3+ y (n = 276)	1.74 (1.26-2.41)	.001	1.42 (1.00-2.01)	.048
Eczema until age 10 y (n = 65)	3.40 (1.98-5.83)	<.001	2.53 (1.41-4.54)	.002
Emotional symptoms				
Eczema in infancy (presence vs absence)				
Only in infancy (age 1-2 y)	1.61 (1.13-2.97)	.01	1.55 (1.07-2.29)	.02
Eczema until age 3+ y	1.92 (1.42-2.59)	<.001	1.67 (1.22-2.30)	.002
Eczema until age 10 y	3.04 (1.79-5.18)	<.001	2.44 (1.39-4.27)	.002
Conduct problems				
Eczema in infancy (presence vs absence)				
Only in infancy (age 1-2 y)	1.96 (1.33-2.87)	.001	1.75 (1.18-2.60)	.005
Eczema until age 3+ y	1.09 (0.73-1.64)	.66	0.96 (0.63-1.46)	.86
Eczema until age 10 y	1.25 (0.58-2.65)	.57	1.07 (0.49-2.34)	.88
Hyperactivity/inattention				
Eczema in infancy (presence vs absence)				
Only in infancy (age 1-2 y)	1.48 (1.00-2.20)	.048	1.38 (0.92-2.08)	.12
Eczema until age 3+ y	1.24 (0.86-1.79)	.24	1.03 (0.69-1.53)	.88
Eczema until age 10 y	1.20 (0.59-2.46)	.62	0.88 (0.40-1.95)	.75
Peer problems				
Eczema in infancy (presence vs absence)				
Only in infancy (age 1-2 y)	1.10 (0.66-1.83)	.707	0.93 (0.55-1.56)	.779
Eczema until age 3+ y	1.10 (0.71-1.73)	.664	0.85 (0.53-1.36)	.503
Eczema until age 10 y	2.09 (1.05-4.19)	.037	1.41 (0.67-2.94)	.366

*SDQ: cutoff between “unlikely” and “possible” as the threshold for identification of psychopathologies (Foreman 2008).³¹

†Adjusted for sex, geographical area, interventional arm, parental education, single parent at age 10 y, breast-feeding, infant eczema, allergic rhinitis (ever), and allergic asthma (ever).

care.²⁵ The SDQ relies only on perceptions of the parents and not on potential differential access to health care, so information bias in the assessment of the outcome of interest is not an issue in our study.

Another strength of our study is the adjustment for a broad set of prespecified confounders including sociodemographic characteristics, breast-feeding, living with a single parent, and atopic comorbidity.^{1,6,7,19} However, the fact that children with more severe eczema have a higher risk of developing allergic asthma and allergic rhinitis than children with mild eczema²⁶ may have introduced overadjustment with consecutive bias of the investigated association between eczema and psychopathologic difficulties toward the null.²⁷

A limitation of our study is that the SDQ was assessed only at a single point in time—that is, at age 10 years—so the psychological and behavioral development was not captured over time. Our study therefore only allows us to draw conclusions about mental health problems at age 10 years in relation to eczema and its course. However, psychopathology is a phenomenon with substantial developmental aspects. Also, the SDQ is a screening questionnaire that must not be equated with a full mental health evaluation.

Despite these limitations, we believe that our study allows us to conclude that eczema precedes and potentially induces psychological difficulties. However, we cannot rule out that another as yet unknown factor may be related to both the manifestation of eczema and the development of mental health problems.

Eczema is one of the most frequent reasons for sleeping problems in children and adolescents.²⁸ Short sleep duration has

been shown to induce behavioral problems in healthy children.²⁹ One limitation of our study is the lack of data on the severity of eczema based on a validated measurement.³⁰

Aiming for a homogeneous study population, we included only healthy newborns of German nationality. Children with low socioeconomic status are overrepresented in those lost to follow-up. Generalizability to the general population may therefore be limited.

Implications for current clinical practice and public health

Our study has significant relevance for clinical practice because it highlights that the spectrum of comorbidities of children with eczema extends far beyond allergies into the realm of psychopathology. With longer duration of eczema persistence, emotional problems become more and more prominent, which might lead to clinically relevant depression in a subgroup of patients. Early and successful prevention of eczema thus becomes all the more important.

Implications for future research

On the basis of the results of this study, future studies should repeatedly administer the SDQ and should aim to incorporate psychological evaluation by a mental health professional.

Future experimental and clinical research is necessary to understand better the underlying biological mechanisms related to eczema in early childhood that cause behavioral problems and

emotional difficulties in subsequent life. In this regard, sleeping problems in infancy should be considered as 1 potentially important explanatory factor. In addition, future studies should evaluate collaborative care models of dermatologists and mental health specialists to optimize medical care for patients with eczema.

In summary, our study indicates that infant eczema—even if cleared later in childhood—has to be considered an important reason for subsequent mental health problems.

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Clinical implications: Children with a history of infant-onset eczema should be considered at risk for mental health problems.

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