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ORIGINAL ARTICLE

Educational, labour market and relationship outcomes in people with acne

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Abstract

Background: Although acne is associated with scarring, mental health comorbidities and bullying, little is known about its impact on socio-economic outcomes.

Objectives: To examine the association between acne and educational, labour market and relationship outcomes.

Methods: We conducted a nationwide registry-based cohort study in Denmark. We included birth cohorts from 1982 to 1988 and compared those with and without acne identified using hospital diagnosis codes and redeemed prescriptions. Our main educational outcome was educational attainment. The main labour market outcomes were earned income at age 30 and long-term unemployment at any time before age 30. The main relationship outcomes were single partnership and childlessness by age 30. Outcomes were assessed using Poisson regression for binary outcomes and linear regression for continuous outcomes, adjusted for sex, calendar year, mother's socio-economic position and hormonal contraception use.

Results: Those with acne had a lower risk of not completing upper secondary education (relative risk (RR): 0.79; 95% confidence interval [CI]: 0.76–0.83) and higher education (RR: 0.90; 95% CI: 0.88–0.91), with absolute differences up to 4 percentage points. Persons with acne had slightly higher income (mean percentile difference: 2.6%, 95% CI: 2.2–2.9) and lower risk of long-term unemployment than those without acne (9.8% vs. 11.4%; RR: 0.90; 95% CI: 0.87–0.93). The prevalence of being single until age 30 was similar (19.7% vs. 20.1%; adjusted RR: 0.96; 95% CI: 0.94–0.98) but childlessness was slightly more prevalent (60.5% vs. 57.5%; adjusted RR: 1.03; 95% CI: 1.02–1.04). However, all associations were attenuated or lost in secondary analysis restricted to exposure-discordant siblings to address confounding from family-related factors.

Conclusions: Acne during adolescence does not seem to affect long-term educational, labour market or relationship outcomes. However, there is a need for additional studies to validate the findings in untreated patients and different health and social systems.

INTRODUCTION

Acne is associated with negative mental health outcomes, including reduced self-esteem, depression and suicidality.[1–4] At school, those with acne describe that they are not thriving and are having difficulty with bullying.[1,5,6] In the workplace, those with acne report feeling their acne makes them appear younger and less professional, trustworthy or qualified.[1,7,8] Those with acne also report social isolation and self-consciousness in their relationships.[1,9] It is possible that stigmatizing attitudes toward those with acne cause challenges at school, work and in relationships.[10] Low self-esteem and bullying have been linked to reduced academic achievements.[11,12] Furthermore, acne may negatively

affect labour market attachment and income due to stigmatization as well as lower educational attainment.[10] Social isolation may reduce the likelihood of partnership or having children.[10]

Nevertheless, little is known about whether acne negatively affects socio-economic outcomes in the long term. Such associations would have important public health implications considering that educational attainment and socio-economic position are associated with overall health and well-being.[13] In this cohort study, we used routinely collected data from nationwide Danish health and social registries to examine the association between acne and educational, labour market and relationship outcomes.

Key points

Why Was the Study Undertaken?

Acne is associated with permanent scarring, mental health comorbidities and stigmatization. People with acne report that their disease negatively influences their school, work and personal lives. However, little is known about its impact on long-term socio-economic outcomes.

What Does this Study Add?

In this registry-based Danish cohort study, acne was associated with positive educational and labour market outcomes and potentially negative relationship outcomes at age 30. However, secondary analyses comparing exposure-discordant siblings to account for family-related confounding could not confirm these associations.

What Are the Implications of this Study for Disease Understanding and/or Clinical Care?

Acne during adolescence does not seem to affect long-term educational, labour market or relationship outcomes. However, there is a need for additional studies to validate the findings in untreated patients and different health and social systems.

MATERIALS AND METHODS

Setting

Denmark's welfare system provides tax-financed healthcare, education and a variety of social services.[14] Costs of prescription drugs are partially reimbursed. The educational system is open and free to all students, including at university level. Social welfare is supported by student aid, disability pensions and benefits, such as unemployment insurance. Health and socio-economic data are recorded in nationwide registries that can be linked using unique personal identifiers.[14]

We based the study on the Medical Birth Registry, which includes data on all births in Denmark.[15] We obtained linked data with information on demographics and kinship from the Civil Registration System,[16] hospital inpatient, outpatient clinic and emergency room diagnoses from the Danish National Patient Registry and Psychiatric Central Research Registry,[17,18] redeemed prescription drugs from the Danish National Prescription Registry,[19] in vitro fertilization (IVF) treatment from the IVF registry[20] and education and labour market outcomes from multiple registries maintained by Statistics Denmark.[21–23]

A description of the study's conceptual framework is described in Appendix S1 and its setting and data sources in Appendix S2.

Study cohorts

A study design diagram is provided in Figure 1 and flowcharts in Figure S1. We first restricted the study to the birth cohorts of 1982–1988 to ensure minimum age of 30 years by the end of follow-up (31 December 2018) and then applied outcome-dependent eligibility criteria to generate study cohorts with individual baseline dates suitable for examining the association between acne and the following variables: (1) lower secondary education (baseline: 13th birthday), (2) upper secondary education (baseline: graduation date from lower secondary education), (3) higher education (baseline: graduation date from upper secondary education) and (4) labour market and relationship outcomes (baseline: 18th birthday). Of note, a secondary analysis of academic performance at lower secondary school included a larger cohort, because data availability and shorter follow-up until age 18 allowed us to include more birth cohorts (1986–2000). We excluded persons with missing covariate information and, for education outcomes, those with a non-consecutive record of education (e.g. higher education recorded before upper secondary education).

Acne definition

We defined acne as an inpatient or outpatient hospital encounter with an acne diagnosis code *or* based on relevant prescriptions, that is, a prescription for topical acne medication, prescriptions for ≥90 pills of oral tetracycline-class antibiotics within 6 months or an isotretinoin prescription before baseline as defined above. We included the prescription-based definition to capture acne treated in general and private practice where clinical data are not routinely recorded. We had at least 1 year of registry data to ascertain exposure. Because the baseline date changed between study cohorts, persons could move from

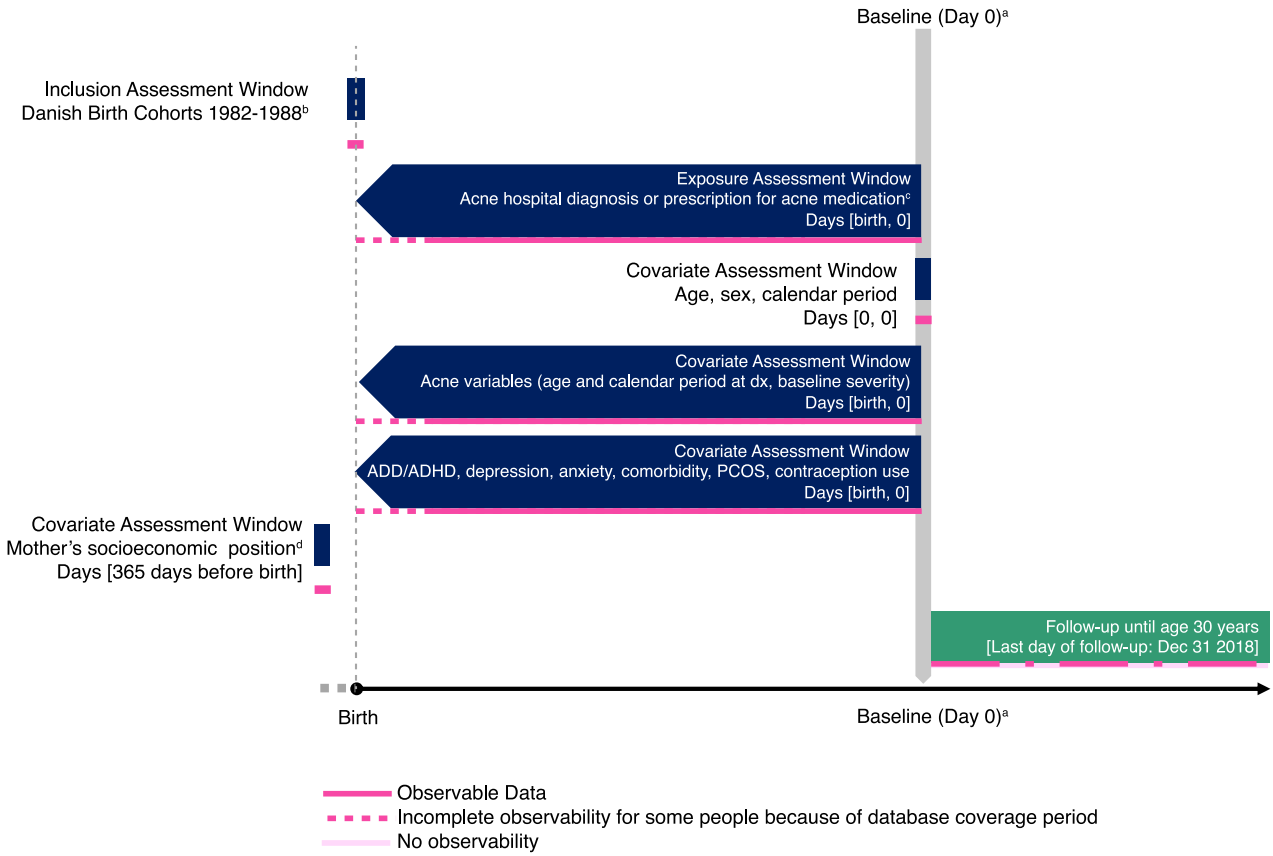

FIGURE 1 Design diagram. [a]Baseline dates and outcomes: Thirteenth birthday for *lower secondary education* and *grade point average* as outcomes. The date of completing lower secondary education for 'upper secondary education' as an outcome. The date of completing upper secondary education for 'higher education' as an outcome. Eighteenth birthday for labour market and relationship outcomes. To ensure sufficient follow-up and lag time between acne exposure and outcome, we included those who had completed lower secondary education before the 27th birthday for assessing upper secondary education and those who had completed upper secondary education before the 25th birthday for assessing higher education. [b]For lower secondary education as an outcome, the 1982 birth cohort was excluded, as we could not assess exposure status before the 13th birthday (prescription data available from 1 January 1995). For assessing grade point average in 9th grade, we included birth cohorts 1986–2000, which ensured that the cohort reached age 16 (when most start 9th grade) in the school year 2001/2002 (when grade data were available) and at least age 18 by the end of follow-up. [c]Acne defined as either an inpatient or outpatient hospital encounter with a diagnosis code for acne, a prescription for topical acne medication, a prescription for isotretinoin or prescription of a total of 90 pills or more of oral tetracycline-class antibiotics within 6 months. [d]If information on the mother's income, education or employment was not available 1 year before the child's birth, then we used the closest available information up to age 13.

unexposed to exposed status for the different outcomes. To reduce misclassification of competing indications, we did not include single-agent topical clindamycin and azelaic acid and shorter treatment courses of tetracyclines (used for e.g. Lyme disease and chlamydia). However, we disregarded the tetracycline tablet dose to capture possible low-dose acne treatment. Appendix S3 provides definitions of all study variables.

As a secondary aim, we performed analyses by acne severity, defined at baseline as mild acne (topical medication use only) or moderate-to-severe acne (hospital diagnosis or systemic acne treatment).

To control for unmeasured confounding from stable family characteristics, we conducted a secondary analysis including full siblings without acne at the specified baseline as unexposed (i.e. exposure-discordant siblings). Because eligibility criteria from the main analysis applied, including a minimum attained age of 30 years, siblings could have a difference of up to 7 years of age.

Outcomes

We followed the cohorts to examine various indicators of socio-economic position by age 30. Our main educational outcome was educational attainment, categorized as lower secondary education (basic, compulsory schooling), upper secondary education and higher education based on the main groups in the Danish nomenclature for education (corresponding largely to the International Standard Classification of Education).[21] We defined the outcome as *not achieving* a specific educational level. As a secondary outcome, we included the grade point average on the 9th-grade final exams (usually completed in the 16th birth year) in Danish and mathematics, to reflect academic performance in central humanistic and scientific areas. We considered both the actual grade point average (continuous variable) and whether one or more exams were not passed (binary). We also examined the prevalence of not attempting all 9th-grade exams in Danish and mathematics by age

18, as this could represent missingness due to illness or other exemptions.

Our main labour market outcomes were earned income (total annual net salary) at age 30 and long-term unemployment (unemployment during at least 50% of a given year) at any time before age 30. We measured earned income as the percentile rank of earned income, using the income distribution for the entire study population within strata of age, sex and calendar year as a reference, to account for inflation. To check for consistency, we also included a binary variable for income in the lower quartile of the income distribution; any history of economic self-sufficiency (yearly income from all available sources, including social benefits, above the 'minimum level' set by Statistics Denmark); non-health-related unemployment; health-related work absenteeism; and receipt of sick leave benefits by age 30. Of note, short-term sick leave spells are not captured.

As measures of relationships, we included single partnership status (never married/cohabitating) and childlessness (having no children) by age 30. As a secondary outcome for assessing childlessness, we included having ever had IVF treatment by age 30.

Most outcome data were interval-censored with yearly updates. In case of missing data in a given year or loss to follow-up, we used the value from the most recent available year.

Covariables

We obtained information on the following indicators of the socio-economic position of participants' mothers: income rank (categorized as below 25th percentile, 25th–75th percentile or above 75th percentile); education level (lower secondary, upper secondary or higher education); and employment status (unemployed, outside workforce or employed). We also included information on ever-use of combined hormonal contraception and progestin-only contraception at baseline. For adjustment in sensitivity analyses, we included polycystic ovary syndrome, depression, anxiety disorder, attention deficit disorder, any non-psychiatric comorbidity according to the Charlson Comorbidity Index and sibling birth order.

Statistical analyses

We compared baseline characteristics in cohorts with and without acne. We used Poisson regression to compute the prevalence ratios as measures of relative risks (RRs) with 95% confidence intervals (CIs) for binary outcomes among people with acne compared with those without. We chose a Poisson model because most outcomes were common and because it allowed us to condition on sibship in the secondary analysis.[24] We compared the mean difference of the grade point average in Danish and mathematics (combined and separately) and the mean percentile (rank) of earned income using the identity function as the link function to fit a generalized linear model that could condition on family in the sibling analysis.[25] To account for potential *heteroscedasticity* and non-*normal* distribution of errors, we computed confidence intervals with the percentile bootstrap method based on 1000 samples which showed symmetric distribution. For all outcomes, we fitted an unadjusted model and a model adjusting for sex, calendar period at baseline, the mother's income and education level and hormonal contraception. Maternal employment status was not included because it correlates strongly with income. For academic performance, we also adjusted for the calendar year of examination. We did not adjust for age, as it did not vary per study design. Based on data availability, we restricted the analyses of non-health-related unemployment, health-related work absenteeism and sick leave benefits to persons whose baseline occurred after July 1991.

To capture potential age trends, we plotted the prevalence of the main outcomes by age according to exposure status. For earned income, we used the median annual real income (converted to Danish 2015 currency values from the World Bank) standardized to income at age 18 years = 100. This analysis excluded people with missing or zero income at age 18 (15% exposed; 17% unexposed). We repeated all analyses among exposure-discordant siblings, conditioning on the family to allow within-family comparisons.

We stratified results by subgroups of age at acne diagnosis (<13 years; ≥13 years), sex, acne severity and the mother's income and educational level. We performed sensitivity analyses to address, for example, impact of other chronic diseases (e.g. depression), misclassification of acne and outcome and residual confounding by the mother's socio-economic position (Appendix S4).

We conducted analyses using SAS 9.4.

RESULTS

We included 264,045 persons (1593 [0.6%] with acne at baseline of age 13) in the cohort for lower secondary education as an outcome, 874,197 (11,471 [1.3%] with acne) in the group for which grade point average was ascertained, 299,668 (15,542 [5.2%] with acne) in the cohort for upper secondary education as an outcome, 242,049 (30,862 [12.8%] with acne) in the cohort for higher education as an outcome and 311,681 (28,181 [9.0%] with acne) for labour market and relationship outcomes (Table 1). The prevalence of acne could differ across cohorts because of varying age at baseline (between 13 and 27 years). Most acne exposed were identified by a redeemed prescription for a topical agent (Table 1). Mothers of those who had acne had higher income, educational level and employment status than mothers of those without acne.

The main analysis showed that persons treated for acne had a lower prevalence of *not* completing upper secondary education (adjusted RR: 0.79; 95% CI: 0.76–0.83) and higher

TABLE 1 Characteristics of persons with and without acne in cohorts used to examine association with lower secondary education, academic performance, upper secondary education, higher education and labour market and relationship outcomes.[a]

	Lower secondary education				Academic performance				Upper secondary education				Higher education				Labour market and relationship outcomes			
	With acne		Without acne		With acne		Without acne		With acne		Without acne		With acne		Without acne		With acne		Without acne	
	N	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%
Total	1593	100	262,452	100	11,471	100	862,726	100	15,542	100	284,126	100	30,862	100	211,187	100	28,181	100	283,500	100
Age at baseline, median (IQR)	13 (13–13)		13 (13–13)		13 (13–13)		13 (13–13)		16.0 (15.8–16.3)		16.0 (15.7–16.2)		20.0 (19.3–20.9)		20.0 (19.2–20.9)		18 (18–18)		18 (18–18)	
Age at acne diagnosis[b]																				
Median (IQR)	12.4 (11.812.7)				12.2 (11.4–12.7)				14.8 (13.9–15.4)				16.4 (15.0–17.9)				15.8 (14.6–16.8)			
<13 years	1593	100	NA		11,471	100	NA		1583	10.2	NA		1353	4.4	NA		1627	5.8	NA	
13+ years	NA		NA		NA		NA		13,959	89.8	NA		29,509	95.6	NA		26,554	94.2	NA	
Sex																				
Female	1185	74.4	126,889	48.3	8428	73.5	416,619	48.3	7618	49.0	138,558	48.8	14,036	45.5	108,519	51.4	12,693	45.0	138,857	49.0
Male	408	25.6	135,563	51.7	3043	26.5	446,107	51.7	7924	51.0	145,568	51.2	16,826	54.5	102,668	48.6	15,488	55.0	144,643	51.0
Year of acne diagnosis																				
1995–1997	451	28.3	NA		123	1.1	NA		2143	13.8	NA		1857	6.0	NA		2236	7.9	NA	
1998–2000	1003	63.0	NA		1256	10.9	NA		6652	42.8	NA		8813	28.6	NA		10,192	36.2	NA	
2001–2003	139	8.7	NA		1598	13.9	NA		6030	38.8	NA		11,316	36.7	NA		11,122	39.5	NA	
2004–2006	NA		NA		8494	74.0	NA		717	4.6	NA		8876	28.8	NA		4631	16.4	NA	
Setting for first acne diagnosis																				
Hospital	15	0.9	NA		69	0.6	NA		91	0.6	NA		144	0.5	NA		137	0.5	NA	
Prescription fill[c]	1579	99.1	NA		11,411	99.5	NA		15,463	99.5	NA		30,744	99.6	NA		28,063	99.6	NA	
Topical agent	1367	85.8	NA		10,470	91.3	NA		9859	63.4	NA		17,453	56.6	NA		16,286	57.8	NA	
Tetracycline	155	9.7	NA		880	7.7	NA		4319	27.8	NA		10,666	34.6	NA		9169	32.5	NA	
Isotretinoin	75	4.7	NA		247	2.2	NA		1905	12.3	NA		4160	13.5	NA		3903	13.8	NA	
ADHD, depression or anxiety disorder	<5		684	0.3	157	1.4	12,660	1.5	61	0.4	909	0.3	182	0.6	859	0.4	142	0.5	1388	0.5
PCOS	0	0	<5		7	0.1	22	0.0	7	0.0	28	0.0	45	0.1	153	0.1	24	0.1	98	0.0
Combined hormonal contraception	12	0.8	373	0.1	155	1.4	2258	0.3	2435	15.7	37,090	13.1	11,693	37.9	88,413	41.9	8704	30.9	92,680	32.7
Progestin-only contraception	<5		10	0.0	8	0.1	130	0.0	26	0.2	540	0.2	423	1.4	2569	1.2	174	0.6	1960	0.7

(Continues)

TABLE 1 (Continued)

	Lower secondary education				Academic performance				Upper secondary education				Higher education				Labour market and relationship outcomes			
	With acne		Without acne		With acne		Without acne		With acne		Without acne		With acne		Without acne		With acne		Without acne	
	N	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%
Non-psychiatric comorbidity[d]	93	5.8	12,522	4.8	1034	9.0	68,302	7.9	958	6.2	15,508	5.5	2143	6.9	13,132	6.2	1868	6.6	17,253	6.1
Mother's income level																				
Low (<Q1)	177	11.1	32,740	12.5	2085	18.2	146,966	17.0	1718	11.1	35,440	12.5	3241	10.5	23,257	11.0	3203	11.4	36,259	12.8
Medium (Q1-Q3)	902	56.6	148,456	56.6	6109	53.3	480,274	55.7	8915	57.4	159,734	56.2	17,814	57.7	120,767	57.2	16,018	56.8	159,075	56.1
High (>Q3)	514	32.3	81,256	31.0	3277	28.6	235,486	27.3	4909	31.6	88,952	31.3	9807	31.8	67,163	31.8	8960	31.8	88,166	31.1
Mother's education level																				
Lower secondary education	483	30.3	86,670	33.0	2722	23.7	234,703	27.2	4359	28.0	92,413	32.5	7405	24.0	57,425	27.2	7648	27.1	95,016	33.5
Upper secondary education	694	43.6	111,370	42.4	5746	50.1	417,582	48.4	6788	43.7	121,328	42.7	13,890	45.0	95,000	45.0	12,361	43.9	119,751	42.2
Higher education	416	26.1	64,412	24.5	3003	26.2	210,441	24.4	4395	28.3	70,385	24.8	9567	31.0	58,762	27.8	8172	29.0	68,733	24.2
Mother's employment status																				
Unemployed	198	12.4	36,514	13.9	1232	10.7	104,034	12.1	1925	12.4	38,918	13.7	3299	10.7	24,999	11.8	3354	11.9	39,981	14.1
Out of the workforce	116	7.3	21,535	8.2	1545	13.5	105,402	12.2	1108	7.1	23,387	8.2	2091	6.8	14,804	7.0	2134	7.6	24,050	8.5
Employed	1279	80.3	204,403	77.9	8694	75.8	653,290	75.7	12,509	80.5	221,821	78.1	25,472	82.5	171,384	81.2	22,693	80.5	219,469	77.4

Abbreviations: IQR, interquartile range; PCOS, polycystic ovary syndrome.

[a]See Figure 1 for details of the definition of cohorts and covariate assessment. Note that age at baseline was 13 years for everyone in the cohorts for outcomes of lower secondary education and grades and 18 years for the labour market and relationship outcome.

[b]Acne diagnosis date was defined as the first (1) date of hospital encounter with a diagnosis code for acne, (2) date of the first prescription for a topical acne medication, (3) date when a person redeemed a total of at least 90 pills of oral tetracycline-class antibiotics within a 6-month period or (4) date of the first prescription redemption of isotretinoin.

[c]Types of acne drugs do not add up to 100%, because a person can redeem more than one type of drug on the same day.

[d]According to the Charlson Comorbidity Index.

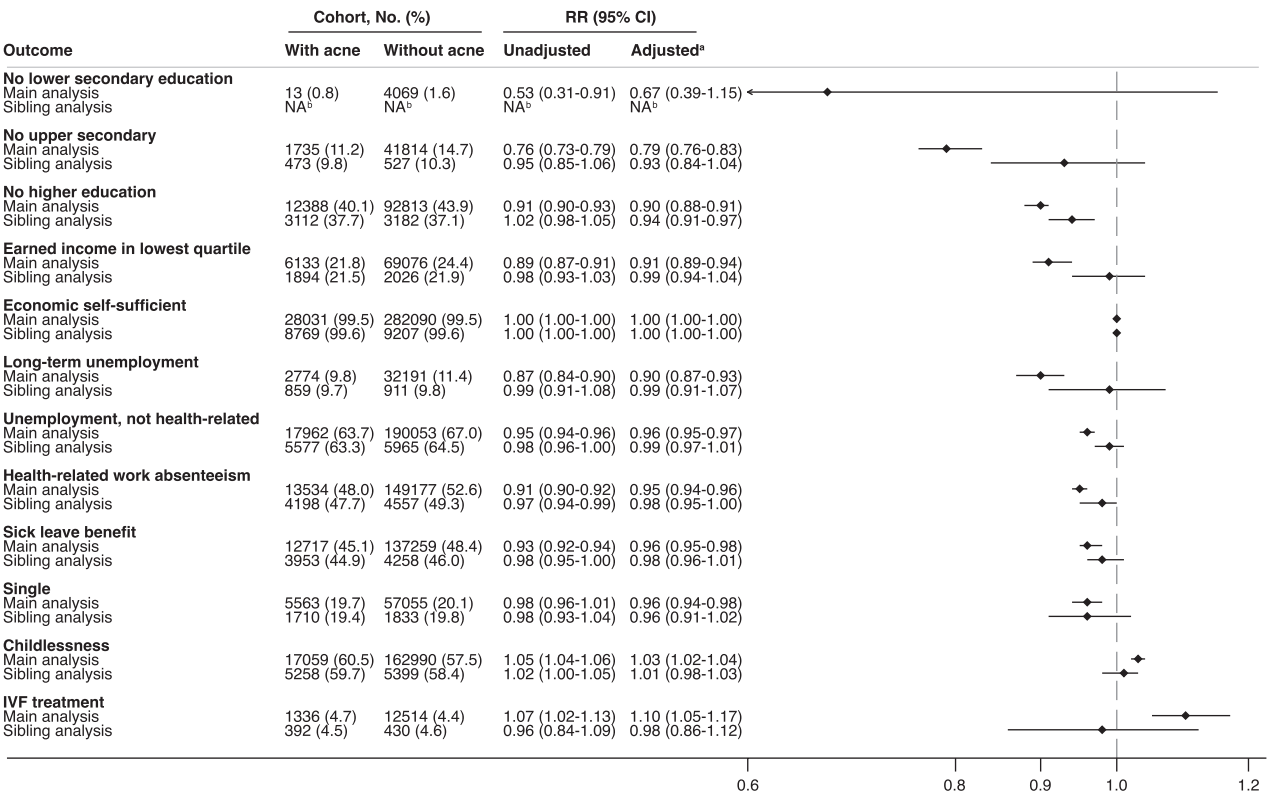

FIGURE 2 Socio-economic outcomes by age 30 in persons with acne compared with persons without acne (main analysis) and siblings without acne (secondary analysis). [a]Adjusted for sex, calendar period at baseline, combined hormonal contraception, progestin-only contraception and the mother's income and education level. [b]Not reported due to a low number of outcomes ($n < 5$) among those with acne.

TABLE 2 Comparison of mean grade of the 9th-grade final exam in persons with acne compared to persons without acne (main analysis) and siblings without acne (secondary analysis).

	With acne		Without acne		Mean grade difference (95% CI)	
Outcome	No. at risk	Mean grade point average (SD)	No. at risk	Mean grade point average (SD)	Unadjusted	Adjusted[a]
Main analysis						
Average of Danish and mathematics	10,411	7.0 (2.50)	762,485	6.6 (2.51)	0.42 (0.38–0.47)	0.16 (0.12–0.21)
Danish	10,411	7.3 (2.45)	762,485	6.6 (2.49)	0.69 (0.65–0.74)	0.26 (0.22–0.31)
Mathematics	10,411	6.8 (3.08)	762,485	6.6 (3.08)	0.15 (0.09–0.21)	0.06 (0.00–0.11)
Sibling analysis						
Average of Danish and mathematics	6097	7.1 (2.48)	7587	6.8 (2.47)	0.24 (0.16–0.33)	0.08 (0.00–0.16)
Danish	6097	7.3 (2.45)	7587	6.8 (2.47)	0.52 (0.43–0.59)	0.15 (0.07–0.23)
Mathematics	6097	6.9 (3.07)	7587	6.9 (3.01)	−0.03 (−0.13–0.08)	0.00 (−0.10–0.11)

[a]Adjusted for sex, calendar period at baseline and examination, combined hormonal contraception, progestin-only contraception and the mother's income and education level.

education (adjusted RR: 0.90; 95% CI: 0.88–0.91), with absolute differences of up to 4 percentage points (Figure 2).

The differences were driven by the higher prevalence of attaining general upper secondary and long-cycle higher education among persons with acne (Table S1). There was also a numerically lower relative risk of not completing lower secondary education (adjusted RR: 0.67; 95% CI: 0.39–1.15) but the estimate was statistically imprecise and the difference in prevalence was small (0.8% vs. 1.6%). Persons with acne had a lower prevalence of not attempting any exam in Danish and mathematics (adjusted RR: 0.91; 95% CI: 0.84–0.97) (Table S2). Among persons who attempted all exams in both subjects, we observed a lower risk of failing at least one exam in those with versus without acne (8.2% vs. 11.2%; adjusted

RR: 0.87; 95% CI: 0.82–0.93), which was explained by grades on the Danish exams. However, we found little difference in the mean grade point average on an absolute scale (overall adjusted mean difference 0.16; 95% CI: 0.12–0.21) (Table 2).

The mean percentile rank of earned income was slightly higher among persons with acne, with an adjusted mean percentile difference of 2.6 (95% CI: 2.2–2.9) (Table S3). The difference in income became apparent after age 25 (Figure S2). There was also a lower risk of ever having experienced long-term unemployment (9.8% vs. 11.4%; RR: 0.90; 95% CI: 0.87–0.93) (Figure 2). Similar associations were observed for the other labour market outcomes. In both the acne and non-acne cohorts, most were economically self-sufficient by age 30 (Figures 2 and S2).

Although the main analysis showed no substantial association between acne and partnership status, acne patients had a lower prevalence of having ever had a partner in younger adulthood (Figures 2 and S2). Acne patients also had a slightly higher prevalence of childlessness (60.5% vs. 57.5%; adjusted RR: 1.03; 95% CI: 1.02–1.04) and IVF treatment (4.7% vs. 4.4%; adjusted RR 1.10; 95% CI: 1.05–1.17) (Figure 2). Stratified analyses by sex suggested that only female patients had an increased prevalence of being single (15.8% vs. 14.8%; adjusted RR: 1.07; 95% CI: 1.02–1.11) and childless (53.2% vs. 48.9%; adjusted RR: 1.06; 95% CI: 1.05–1.08) up to age 30, while no notable subgroup differences were found for other outcomes (Tables S4 and S5).

In the sibling analysis, the number of exposed and unexposed persons were 428 out of 446 for lower secondary education as an outcome, 6636 out of 8351 for the grade analysis, 4838 out of 5113 for upper secondary education, 8255 out of 8583 for higher education and 8805 out of 9249 for labour market and relationship outcomes. All associations in the sibling analysis were attenuated, showing no substantial absolute or relative difference for any outcome (Figures 2 and S3, Tables 2, S2, S3 and S6).

Results were robust in all sensitivity analyses (data not shown).

DISCUSSION

In this large cohort of individuals treated for acne, we found that acne was associated with positive educational and labour market outcomes and potentially negative relationship outcomes. However, the absolute differences were small, and the associations were attenuated or lost when comparing exposure-discordant siblings. As the latter analysis controls better for family-level confounders, these findings suggest overall that acne is unlikely to have a substantial association with socio-economic prospects.

There are only a few previous studies on this topic. In a study based on the National Longitudinal Study of Adolescent to Adult Health, which sampled over 90,000 US students in Grades 7–12, those who reported skin problems, such as itching or pimples in Grades 7–12, had higher grades and a greater likelihood of completing a college degree.[26] Skin problems were also associated with feeling less socially accepted and less attractive, and with lower participation in athletics and increased participation in non-sports clubs. The authors hypothesized that stigmatization due to skin problems could shift focus to intellectual pursuits.[26]

Another study found that the prevalence of unemployment was higher among persons with active acne at ages 18–30 ($n = 625$) compared with age- and sex-matched controls ($n = 625$).[27] An important difference between that study and ours is its requirement for active acne when the outcome was assessed and the older age of participants. It is possible that stigmatization of adolescents with acne results in a focus on educational attainment and thus ultimately lower unemployment rates, while in adults it could lead to adverse labour market outcomes.[1,7,8,10]

Although our findings suggest a neutral to potentially positive association between acne and educational and labour market outcomes, this does not diminish the importance of medical care for those with acne. Acne can be associated with permanent scarring and mental health challenges, including reduced self-esteem, social isolation, sleep impairment, depression, anxiety and suicidal ideation.[1,28–30]

Our study has several strengths, including its large size with over 30,000 individuals with acne, long-term and near-complete follow-up and the ability to evaluate multiple socio-economic outcomes using data from the comprehensive Danish registries.[14] In addition, the sibling analysis reduced potential confounding due to family-related factors. It is a limitation that not all individuals with acne seek medical care, as suggested by a prevalence of only 10% treated for acne at age 18 using our algorithm. The misclassification of untreated acne patients as unexposed may have biased our findings toward the null. Alternatively, it could also explain the positive associations observed if acne patients who seek care achieve improved skin appearance upon successful treatment. This also affects the interpretation of severity analyses, and unfortunately, we lacked clinical details on scarring. Although we found no effect modification by the mother's socio-economic position, generalizability to countries with less uniform health and social support systems is uncertain.

The socio-economic data used in our study are considered of high quality.[21–23] Furthermore, our results were robust in sensitivity analyses addressing the issue of missing income data in individual years. However, misclassification of partnership, for example, by excluding partners living apart, is possible and we could not determine outcomes beyond age 30, which particularly affects the interpretability of the relationship outcomes. We also may have missed an impact of acne flares on work absenteeism, as we could not capture short-term sick leave.

Persons from families with a greater focus on health and education may be more likely to seek acne treatment and achieve positive socio-economic outcomes like those observed. Indeed, a study of Ontario residents found that those with higher socio-economic status were more likely to seek care for acne.[31] The discordant findings in the sibling

analysis suggest residual confounding from family-related factors in the main analysis, including childhood socio-economic position and health-seeking behaviour. However, possible limitations of the sibling design should be considered, including reduced power, unmeasured confounding from factors that vary between exposure-discordant siblings, and possible cross-sibling effects.[32,33] We note that adjustment for sibling differences in calendar year and birth order did not affect estimates. Exposure misclassification could also be of particular concern if affected siblings share acne treatments; however, excluding unexposed siblings had no impact on the main results.

In conclusion, our primary analysis found that by age 30 acne was associated with positive educational and labour market outcomes and potentially negative relationship outcomes. However, secondary analyses accounting further for family-related factors did not find evidence for the association of acne with any of the socio-economic outcomes. There is a need for additional studies to delineate the potential association observed and the generalizability to untreated patients and settings with different health and social systems.

AUTHOR CONTRIBUTIONS

John Barbieri: Conceptualization-lead, funding acquisition-supporting, investigation-lead, methodology-lead and writing—original draft-lead. Dóra Farkas: Conceptualization-supporting, data curation-lead, formal analysis-lead, investigation-supporting, methodology-lead, supervision-equal and writing—review and editing-equal. Niels Skipper: Conceptualization-supporting, investigation-supporting, methodology-supporting, supervision-equal and writing—review and editing-equal. Ketaki Bhate: Conceptualization-supporting, funding acquisition-supporting, investigation-supporting, methodology-supporting, supervision-equal and writing—review and editing-equal. Sinead Langan: Conceptualization-supporting, funding acquisition-supporting, investigation-supporting, methodology-supporting, supervision-equal and writing—review and editing-equal. Line Kibsgaard: Conceptualization-supporting, investigation-supporting, methodology-supporting, supervision-equal and writing—review and editing-equal. Henrik Toft Sørensen: Conceptualization-supporting, funding acquisition-supporting, investigation-supporting, methodology-supporting, resources-lead, supervision-equal and writing—review and editing-equal. Sigrun A.J. Schmidt: Conceptualization-lead, funding acquisition-lead, investigation-lead, methodology-lead, project administration-lead and writing—original draft-lead.

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CONFLICT OF INTEREST STATEMENT

John S Barbieri has received consulting fees from Dexcel Pharma for work unrelated to the present study. Sigrun AJ Schmidt has received speaker honoraria from GSK Pharma for lectures unrelated to the present study. Line Kibsgaard has received consulting fees as a speaker from Astra Seneca A/S, Leo-Pharma and Novartis. Dr. Kibsgaard is and has been engaged in clinical trials sponsored by Abbvie, Sanofi, INCB and Galderma, and attended advisory board meetings financed by MSD, Denmark. The rest of the authors declare no relevant conflicts of interest.

DISCLOSURES

The Department of Clinical Epidemiology, Aarhus University, receives funding for other studies in the form of institutional research grants to (and administered by) Aarhus University. None of these studies has any relation to the present study.

DATA AVAILABILITY STATEMENT

No additional unpublished data are available because this study used existing data from the Danish nationwide registries that are accessible only to researchers who fulfil local requirements, following approval by the Danish Data Protection Agency, the Danish Health Data Authority and Statistics Denmark.

ETHICS STATEMENT

The study was reported to the Danish Data Protection Agency by Aarhus University (Record number 2016-051-000001; serial number 605). Danish legislation does not require ethical review board approval or informed consent from subjects in registry-based studies. Results are reported per STROBE and RECORD guidelines.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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