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ORIGINAL ARTICLE

Socioeconomic background affects mortality in Danish children with severe chronic disease

Andreas Jensen[1] | Gorm Greisen[2,3] | Lone Graff Stensballe[1]

[1]Department of Paediatrics and Adolescent Medicine, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark

[2]Department of Intensive Care of Newborns and Small Children, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark

[3]Institute of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark

Correspondence
Andreas Jensen, Department of Paediatrics and Adolescent Medicine, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark.
Email: andreas.jensen.01@regionh.dk

Abstract

Aim: To assess the association between socioeconomic factors and mortality in Danish children diagnosed with different types of severe chronic disease, including cancer.

Methods: National cohort study 1994–2020 including Danish children with chronic disease. Inclusion was based on diagnoses in The National Patient Register, socioeconomic information was obtained from Statistics Denmark and mortality was ascertained from the Cause of Death Register. Hazard ratios (HR) with 95% confidence intervals (CIs) were based on Cox regression. The factors were combined in one common risk score and the association with disease-specific mortality was analysed overall and by ethnicity status.

Results: Overall, non-Danish ethnicity (HR = 1.96 (95% CI 1.69–2.28)) was associated with all-cause mortality in 128 129 children (69 435 male and 58 694 female) with chronic disease. Median age at first diagnosis was 1.42 years (range 0–18 years). Low family income was associated with mortality regardless of ethnicity status, and young maternal age was also a notable risk factor across ethnicities. The socioeconomic association was more pronounced in children with cancer.

Conclusion: In the high-income setting of Denmark, ethnicity and differences in socioeconomic background were associated with child mortality even among children with severe chronic disease. The pattern was more pronounced in paediatric cancer patients.

KEYWORDS
child, chronic disease, mortality, risk score, socioeconomic status

1 | INTRODUCTION

A previous study found that socioeconomic factors affected the all-cause mortality rate in otherwise healthy Danish children.[1] The present study concerns children diagnosed with a severe, potentially life-threatening, chronic disease. When it comes to reducing mortality in patients with life-threatening disease the conventional focus is on healthcare quality. This leads to the introduction of ever more highly specialised treatments with the ambition of improving the quality of diagnosis and treatment.[2–4] However, little is known about the influence of socioeconomic factors on mortality and even less is known about the potential benefits of socioeconomic interventions. Previous studies on the association between socioeconomic factors and cancer survival in Danish children highlighted these aspects.[5,6]

Abbreviations: CI, confidence interval; HR, Hazard ratio; ICD-10, International Classification of Diseases, Tenth Revision.

One study concluded that family background influenced the mortality rate in paediatric cancer patients despite access to standardised and free-of-charge treatment.[7]

The aim of this Danish register study was to build on the existing knowledge by extending the methods to include children with all forms of severe chronic disease. Thus, the associations between socioeconomic factors and mortality in paediatric cancer patients were compared to those of other life-threatening diseases with less standardisation of treatment.

Key Notes

- Knowledge on the association between ethnicity and socioeconomic background and mortality among children with chronic diagnoses beyond cancer was needed.
- The present study among 128 129 Danish children indicated that ethnicity and different socioeconomic factors such as low family income and young maternal age were associated with mortality in children with all types of chronic disease.
- The socioeconomic association with mortality was indeed more pronounced within children diagnosed with cancer.

2 | METHODS

2.1 | Data

The study was based on data from Danish national registers.[8] The background population was all children born in Denmark 1994–2018. Exposure and outcome were ascertained in the period 1994–2020. Children with severe chronic disease were identified in the National Patient Register using specific diagnosis codes registered in relation to hospitalisations. The procedure is described in more detail elsewhere.[1,9] In the present study, the diagnoses were divided into 11 categories of diseases (Table 1) based on the chapters of the International Classification of Diseases, Tenth Revision (ICD-10).[10] The socioeconomic factors are presented in Table 2.

Two versions of the mortality outcome were analysed: total mortality and post-discharge mortality. The latter outcome excluded deaths occurring in the hospital before discharge to the home after birth as some socioeconomic factors may affect mortality differentially in this period.[1,11]

To reduce the dimensionality of the analyses on subcategories of chronic disease, the association between the socioeconomic factors and mortality in children with any chronic disease was used to develop a common socioeconomic risk score applicable for all children in the study (more details in the statistics subsection below). Two versions of each model were fitted: one with ethnicity status, Danish or non-Danish, as a covariate, and one separated by ethnicity, since this factor may indicate socioeconomic position and affect disease severity within some diagnosis categories.[12,13]

The derived risk score was then used as a continuous covariate when analysing mortality within each chronic disease category (Table 1). Finally, the association was contrasted for children with cancer diagnoses versus children with non-cancer diagnoses. These models were analysed overall and by ethnicity status in accordance with the underlying models generating the socioeconomic risk scores.

TABLE 1 Categories of chronic disease

Disease category name
Neoplasms (cancer)
Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism
Endocrine, nutritional and metabolic diseases
Diseases of the nervous system
Diseases of the circulatory system
Diseases of the respiratory system
Diseases of the digestive system
Diseases of the musculoskeletal system and connective tissue
Diseases of the genitourinary system
Certain conditions originating in the perinatal period
Congenital malformations, deformations and chromosomal abnormalities

2.2 | Statistical analyses

2.2.1 | Derivation of risk scores

The risk score was based on two versions of a main model: one overall model and one separated by ethnicity status. All children were followed from the date of initial diagnosis to the first of the following events: death, emigration, 18 years of age or 31 December 2020. The analyses were based on Cox regression with time to death as the outcome and time since diagnosis as the underlying time scale. Each of the socioeconomic factors were included as categorical covariates. Further, the analyses were adjusted for age at diagnosis and calendar time as continuous covariates measured in years and stratified for seasonality. Missing values were handled by allocating a separate covariate level. The risk score was generated using the sum of the individual socioeconomic factors weighted by the estimated coefficients. The result was scaled by log (2) for interpretability: the relative change in mortality rate when the risk score is doubled. The risk score was subsequently used in the analyses of each chronic disease category.

2.2.2 | Socioeconomic background and disease-specific mortality by ethnicity status

For each chronic disease category, the mortality rate was analysed using Cox regression with the risk score as covariate and an interaction term with ethnicity status when relevant. The interpretation of the resulting hazard ratio (HR) is the ratio in mortality rate

TABLE 2 Socioeconomic factors

Name	Levels
Sex	Male, female
Maternal age	<25 years, 25–30 years, 30–35 years, >35 years
Paternal age	<25 years, 25–30 years, 30–35 years, >35 years
Siblings	Yes, no
Living with both parents	Yes, no
Family income (population adjusted to calendar year)	Low 3rd, mid 3rd, high 3rd
Maternal education	Primary, secondary, tertiary
Paternal education	Primary, secondary, tertiary
Maternal job status	Employed, unemployed, out of workforce, student
Paternal job status	Employed, unemployed, out of workforce, student

between two individuals with one having a socioeconomic risk score twice as large as the other. Overlaps were not considered in the sense that children with diagnoses within more than one chronic disease category could contribute to more than one sub-analysis. However, overlap was handled in the direct cancer vs. non-cancer comparison such that the child only belonged to the group in which it was first diagnosed. The contrast in the association between mortality and the socioeconomic risk score was here assessed by introducing an additional interaction term for cancer vs. non-cancer.

All analyses were performed using *Stata/MP 17.0 (StataCorp, Texas, USA)*.

3 | RESULTS

3.1 | Overall chronic disease

The total population comprised 128 129 children with chronic disease of which 11 461 (8.9%) were of non-Danish ethnicity. In the overall analysis, non-Danish ethnicity was associated with increased mortality (HR 1.96, 95% confidence interval (CI) 1.69–2.28). A few of the socioeconomic factors were associated with overall mortality (Table 3). In the main analysis, low family income was overall associated with higher mortality (HR 1.31, 95% CI 1.15–1.50). The estimate of maternal age < 25 years was especially pronounced in the analysis of post-discharge mortality (HR 1.47, 95% CI 0.81–2.65) in the non-Danish ethnicity stratum, albeit with some uncertainty (HR 1.19, 95% CI 0.90–1.57) in the Danish ethnicity stratum.

3.2 | Mortality within categories of chronic disease

The association between the socioeconomic risk score and mortality varied across the different diagnosis categories (Table 4). The strongest association was found within cancer patients: a doubling of the socioeconomic risk score was associated with a more than doubled mortality rate (HR 2.27, 95% CI 2.01–2.56).

Socioeconomic background was also associated with mortality in children with blood disease (HR 1.80, 95% CI 1.35–2.40). The socioeconomic risk score was not as strongly associated with mortality in the group of endocrine, nutritional and metabolic diseases. The same was the case within circulatory, respiratory, genitourinary, digestive, perinatal and congenital diseases. The composite analysis of non-cancer patients also resulted in some increase in the mortality rate for children of Danish (HR 1.70, 95% CI 1.59–1.80) as well as non-Danish ethnicity (HR 2.03, 95% CI 1.75–2.35). In the main analysis, the stronger influence of socioeconomic background in cancer patients was confirmed by the interaction analysis (HR 1.64, 95% CI 1.48–1.83). However, this contrast was less pronounced for post-discharge mortality (HR 1.33, 95% CI 1.20–1.47).

4 | DISCUSSION

To our knowledge, this is the first study to explore the associations between socioeconomic factors and mortality in children with all forms of severe chronic disease. The socioeconomic association with cancer mortality was confirmed. The size of the estimate was smaller for non-cancer diagnoses, but the direction of the association was the same for other disease categories.

Previous studies in Danish children found young maternal age, parents not living together, lower maternal education, number of children in the household and living outside the capital region to be associated with increased cancer mortality.[5–7] The present study was based on the same registers and the findings were more or less replicated. A review from 2018 found socioeconomic factors to be associated with paediatric cancer survival in other high-income countries as well.[14] The fact that cancer just accounted for around 13% of all mortality in children with severe chronic disease (463 of 3521 deaths) highlights the value of the results on all forms of severe chronic disease presented here.

TABLE 3 Mortality hazard ratios for each socioeconomic risk factor in children with severe chronic disease by ethnicity status

Mortality hazard ratios (95% confidence interval)							
Mortality outcome		**Total mortality**			**Post-discharge mortality**		
Number of children		128 129			127 224		
Number of deaths		3521			2639		
Ethnicity status		Overall	Danish	Non-Danish	Overall	Danish	Non-Danish
Risk factors (reference level)	*Baseline %*						
Non-Danish ethnicity	8.9%	1.96 (1.69–2.28)	-	-	1.99 (1.70–2.33)	-	-
Male sex	54.2%	1.01 (0.95–1.08)	1.05 (0.95–1.16)	1.06 (0.83–1.35)	1.01 (0.94–1.09)	1.06 (0.96–1.18)	1.04 (0.81–1.34)
Maternal age (ref > 35 years)							
<25 years	12.3%	1.09 (0.93–1.29)	1.16 (0.89–1.52)	1.39 (0.78–2.49)	1.21 (0.99–1.47)	1.19 (0.90–1.57)	1.47 (0.81–2.65)
25–29 years	28.9%	1.00 (0.87–1.14)	1.05 (0.85–1.30)	1.16 (0.69–1.95)	1.04 (0.88–1.22)	1.06 (0.85–1.32)	1.19 (0.70–2.03)
30–35 years	33.5%	1.01 (0.90–1.14)	0.95 (0.78–1.15)	0.97 (0.59–1.57)	1.03 (0.89–1.19)	0.98 (0.80–1.19)	0.93 (0.56–1.54)
Paternal age (ref > 35 years)							
<25 years	5.7%	0.94 (0.78–1.14)	0.92 (0.68–1.22)	1.35 (0.75–2.45)	0.93 (0.75–1.15)	0.95 (0.71–1.28)	1.34 (0.74–2.43)
25–29 years	20.6%	0.96 (0.85–1.09)	0.94 (0.78–1.14)	1.00 (0.63–1.59)	1.00 (0.86–1.16)	0.95 (0.78–1.15)	1.00 (0.63–1.59)
30–35 years	34.4%	0.97 (0.88–1.08)	0.90 (0.77–1.05)	1.09 (0.75–1.59)	0.98 (0.87–1.11)	0.92 (0.78–1.08)	1.08 (0.73–1.58)
Siblings	45.1%	0.95 (0.87–1.03)	1.16 (1.02–1.32)	1.17 (0.85–1.63)	1.01 (0.92–1.11)	1.17 (1.02–1.33)	1.18 (0.85–1.64)
Not living with both parents	12.0%	1.11 (0.97–1.28)	1.07 (0.91–1.25)	1.04 (0.72–1.51)	1.07 (0.92–1.24)	1.01 (0.86–1.20)	1.01 (0.69–1.47)
Family income (ref: high 3rd)							
Low 3rd	33.9%	1.31 (1.15–1.50)	1.23 (1.05–1.44)	1.32 (0.63–2.80)	1.29 (1.12–1.49)	1.25 (1.06–1.46)	1.25 (0.59–2.66)
Mid 3rd	32.7%	1.02 (0.90–1.16)	0.98 (0.86–1.12)	1.42 (0.65–3.11)	1.01 (0.89–1.15)	0.99 (0.86–1.13)	1.39 (0.64–3.05)
Maternal education (ref: tertiary)							
Primary	0.6%	0.94 (0.66–1.35)	0.71 (0.10–5.07)	0.99 (0.48–2.03)	0.99 (0.66–1.49)	0.75 (0.11–5.38)	0.97 (0.47–1.99)
Secondary	61.5%	1.04 (0.95–1.13)	0.94 (0.82–1.07)	1.31 (0.80–2.15)	1.06 (0.96–1.17)	0.92 (0.81–1.06)	1.25 (0.76–2.06)
Paternal education (ref: tertiary)							
Primary	0.4%	1.05 (0.69–1.60)	2.37 (0.76–7.45)	0.79 (0.36–1.71)	1.08 (0.66–1.78)	2.51 (0.80–7.88)	0.81 (0.37–1.76)
Secondary	64.4%	1.05 (0.95–1.15)	1.04 (0.90–1.19)	1.07 (0.73–1.56)	1.02 (0.92–1.13)	1.03 (0.90–1.19)	1.09 (0.74–1.59)
Maternal job situation (ref: employed)							
Unemployed	4.8%	0.92 (0.80–1.07)	0.87 (0.68–1.10)	1.01 (0.60–1.71)	0.89 (0.75–1.06)	0.87 (0.68–1.11)	1.04 (0.61–1.76)
Out of workforce	17.1%	0.98 (0.89–1.08)	1.04 (0.88–1.21)	1.09 (0.77–1.53)	0.98 (0.88–1.09)	1.03 (0.88–1.21)	1.11 (0.78–1.57)
Student	8.6%	0.98 (0.86–1.12)	1.03 (0.85–1.25)	0.92 (0.47–1.78)	0.96 (0.82–1.12)	1.02 (0.84–1.25)	0.96 (0.49–1.86)

TABLE 3 (Continued)

Mortality hazard ratios (95% confidence interval)							
Mortality outcome		Total mortality			Post-discharge mortality		
Paternal job situation (ref: employed)							
Unemployed	3.2%	0.95 (0.79–1.13)	0.83 (0.61–1.13)	1.16 (0.78–1.75)	0.94 (0.77–1.14)	0.81 (0.59–1.11)	1.19 (0.79–1.79)
Out of workforce	7.9%	0.93 (0.82–1.05)	0.96 (0.77–1.19)	1.02 (0.75–1.39)	0.92 (0.80–1.06)	0.94 (0.75–1.18)	1.02 (0.75–1.40)
Student	4.2%	1.02 (0.86–1.22)	1.05 (0.81–1.34)	0.81 (0.35–1.86)	1.02 (0.83–1.26)	1.02 (0.79–1.32)	0.69 (0.28–1.71)
Continuous covariates							
Age at diagnosis	-	1.12 (1.10–1.14)	1.13 (1.11–1.15)	1.08 (1.03–1.13)	1.12 (1.10–1.14)	1.13 (1.11–1.15)	1.08 (1.02–1.13)
Year of birth	-	0.94 (0.93–0.94)	0.93 (0.92–0.94)	0.95 (0.93–0.97)	0.92 (0.92–0.93)	0.93 (0.92–0.94)	0.95 (0.93–0.97)

Note: Overall and baseline numbers for the main analysis. The overall estimate may not be a weighted average of the two stratum-specific estimates due to different underlying models.

The finding of a larger socioeconomic association with mortality in paediatric cancer patients could be explained by the unevenly distributed parental prerequisites to follow the prolonged, intensive and highly specialised anti-cancer treatments within the healthcare system. Two recent Danish studies offer some explanation as to why socioeconomic background in particular affected the risk of mortality in children with cancer. First, Pedersen et al found lower prescribed doses of anti-cancer medication to children of parents with lower education and unemployment. However, no difference in adherence to the treatment was found.[15] Thus, inferior physician compliance to protocol recommendations of anti-cancer treatment could partly explain the larger social inequality in cancer patients observed in the present study. Second, Pedersen et al found that among Danish children with cancer, families with socioeconomic disadvantage, non-Western origin or depression were more frequent users of pre-diagnostic healthcare services.[16] This indicated that even in the high-income setting of Denmark, some families struggle to navigate in the healthcare system even when their child is severely ill.

The extent of these difficulties remains unclear. Physician compliance to treatment recommendations may also explain social differences in mortality after other severe chronic diagnoses. Although in the present study the socioeconomic differences in mortality were more pronounced in cancer patients, it is important to note that possible inequalities in patients with other diseases should be taken seriously. In the overall model, non-Danish ethnicity was the single factor with the largest impact on the mortality rate, and language as well as cultural factors, on top of economic disadvantage, may present obstacles to the collaboration between the family and the healthcare system.

Many childhood deaths were not covered in the present study. First, death after first discharge to the home after birth in children without a diagnosis of a severe chronic disease also occurs, albeit less frequently.[1] Second, despite low child mortality in Denmark, relatively many children die before discharge to the home without a chronic diagnosis. Prematurity and birth asphyxia are leading causes of child mortality worldwide, and the influence of socioeconomic factors is well-known, also in high-income settings as the Nordic countries, and perhaps especially in Denmark.[15,16] Thus, the present results followed the general pattern to some extent.

One strength of the present study was the national cohort design and large sample size, complete coverage and no loss to follow-up due to the high quality of the Danish health and social registers. One limitation was the fact that training and validation data sets were not used in the model fit prior to the calculation of the risk scores. This choice was made to ensure that the full set of events was exploited in each part of the analysis. Further, there was a minor overlap in the sense that children could contribute to more than one sub-analysis across the different categories of chronic diagnoses. However, the children only contributed with the first occurring diagnosis in the main analysis. Finally, missing data could influence the results given that missingness cannot assumed to be (completely) random.

TABLE 4 Mortality hazard ratios per doubling in socioeconomic risk score by chronic disease category and ethnicity

Mortality hazard ratios (95% confidence interval)							
Mortality outcome		**Total mortality**			**Post-discharge mortality**		
Ethnicity status							
Disease category	***Number of children (deaths) main analysis***	**Overall**	**Danish**	**Non-Danish**	**Overall**	**Danish**	**Non-Danish**
Neoplasms (cancer)	3221 (463)	2.27 (2.01–2.56)	2.65 (2.31–3.04)	2.36 (1.69–3.31)	2.03 (1.81–2.26)	2.16 (1.89–2.48)	2.19 (1.90–2.51)
Diseases of the blood	1410 (75)	1.80 (1.35–2.40)	2.29 (1.63–3.22)	2.03 (1.00–4.13)	1.74 (1.34–2.26)	1.40 (1.01–1.95)	1.43 (1.04–1.98)
Endocrine, nutritional and metabolic	10 439 (230)	1.38 (1.21–1.58)	1.63 (1.34–1.99)	1.90 (1.37–2.63)	1.34 (1.18–1.53)	1.32 (1.14–1.54)	1.34 (1.15–1.56)
Nervous system	25 081 (914)	0.96 (0.89–1.03)	1.08 (0.98–1.19)	1.33 (1.08–1.63)	0.99 (0.93–1.06)	0.91 (0.85–0.99)	0.92 (0.85–0.99)
Circulatory system	9389 (590)	1.16 (1.06–1.27)	1.62 (1.42–1.86)	2.37 (1.76–3.21)	1.26 (1.15–1.37)	1.10 (1.00–1.21)	1.11 (1.01–1.22)
Respiratory system	7468 (57)	1.54 (1.11–2.13)	1.76 (1.19–2.60)	1.73 (0.64–4.73)	1.43 (1.08–1.90)	1.53 (1.03–2.25)	1.63 (1.10–2.41)
Digestive system	24 319 (301)	1.43 (1.26–1.63)	1.53 (1.31–1.80)	1.86 (1.31–2.63)	1.54 (1.36–1.74)	1.42 (1.24–1.64)	1.45 (1.26–1.66)
Musculoskeletal	8508 (15)	0.96 (0.53–1.75)	0.96 (0.48–1.89)	1.97 (0.42–9.21)	1.03 (0.60–1.77)	1.17 (0.60–2.27)	1.07 (0.56–2.04)
Genitourinary system	4558 (92)	1.38 (1.08–1.77)	1.69 (1.20–2.39)	1.89 (1.12–3.18)	1.34 (1.06–1.69)	1.28 (0.97–1.68)	1.32 (1.00–1.74)
Perinatal conditions	4844 (488)	0.94 (0.86–1.03)	1.55 (1.22–1.97)	1.09 (0.61–1.95)	1.12 (0.97–1.28)	0.92 (0.84–1.01)	0.93 (0.85–1.02)
Congenital malformations etc.	50 658 (2116)	1.12 (1.07–1.17)	1.77 (1.59–1.96)	1.93 (1.53–2.43)	1.38 (1.30–1.45)	1.04 (0.99–1.10)	1.05 (1.00–1.11)
All non-cancer	125 958 (3290)	1.18 (1.14–1.22)	1.70 (1.59–1.80)	2.03 (1.75–2.35)	1.36 (1.29–1.42)	1.69 (1.58–1.80)	2.01 (1.73–2.32)
Cancer vs. non-cancer interaction	128 129 (3521)	1.64 (1.48–1.83)	1.73 (1.61–1.86)	1.89 (1.61–2.22)	1.33 (1.20–1.47)	1.73 (1.61–1.86)	1.90 (1.62–2.23)

Note: The overall estimate may not be a weighted average of the two stratum-specific estimates due to different underlying models.

5 | CONCLUSION

In conclusion, in the high-income setting of Denmark, ethnicity and differences in socioeconomic background were associated with mortality in children with severe chronic disease. The social inequality in mortality was largest among children with a cancer diagnosis.

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CONFLICT OF INTEREST

The authors have no conflict of interest to declare.

ORCID

Andreas Jensen https://orcid.org/0000-0003-4302-2982
Gorm Greisen https://orcid.org/0000-0001-8042-3262
Lone Graff Stensballe https://orcid.org/0000-0003-1569-153X

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