Infective endocarditis and the association to income as a proxy for socioeconomic position: A Danish nationwide register-based cohort study

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ABSTRACT

Background Despite continued focus on infective endocarditis morbidity and mortality remains high. Socioeconomic position is known to influence the risk of multiple diseases but the impact on the occurrence of infective endocarditis is unknown. We aimed to investigate the association between available income as a proxy for socioeconomic position and infective endocarditis in an unselected nationwide population.

Methods By cross-linking Danish nationwide registers, we identified all Danish residents above 30 years of age, from January 1, 2007 through December 31, 2017. Information on income, comorbidities and the primary outcome of infective endocarditis was obtained through the registers. Socioeconomic position was defined according to quintiles of disposable income. The association between socioeconomic position and infective endocarditis was examined using multivariate Poisson Regression analyses, incorporating time-updated estimates of disposable income.

Results The study included 3,524,314 individuals (median age = 47 years) with a median follow-up of 11 years. Declining level of income was associated with increasing incidence rates of infective endocarditis, spanning from 7 to 20 events/100,000 person-years. Individuals with low income had higher incidence rate ratio (IRR) of infective endocarditis compared to individuals with high income (lowest vs highest income group, IRR = 1.58 [1.43-1.75]). The association between decreasing income and increasing IRR of infective endocarditis was present across all age groups, although the association was strongest in the young population.

Conclusion In a nationwide population, a significant association between low income and increasing incidence of infective endocarditis was observed. The association was most evident in younger individuals. (Am Heart J 2025;287:119–127.)

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Background

Infective endocarditis (IE) is a life-threatening disease associated with high morbidity and mortality.[1-3] The incidence of IE is increasing in developed countries including Denmark[4-6] and has simultaneously evolved from being a community-acquired disease into gradually becoming a healthcare-related infectious disease.[3,7,8] The diagnosis of IE is often delayed, due to nonspecific symptoms.[9] For this reason, correct antimicrobial treatment may also be delayed, which in turn can affect the prognosis for the IE patient. To improve health outcomes for patients with IE, correct and early diagnosis is of paramount importance along with knowledge of risk factors for developing IE. Previous research on somatic risk factors for IE has revealed multiple associated factors, including

previous diagnosis of IE, heart valve disease, and carrying a cardiac implantable device.[10-13] This has resulted in guideline recommendations for increased focus on specific patient groups, as well as prophylactic antibiotic treatment in individuals at particular high risk of developing IE.[1] Previous studies have focused on somatic risk factors for IE,[10-13] while there is a paucity of research focused on exploring possible associations between nonsomatic risk factors and IE.

Socioeconomic position (SEP), assessed by income and/or educational level, is a well-known risk factor for many diseases, including cardiovascular disease[14] and infectious diseases.[15,16] Therefore, an association between SEP and IE might very well be suspected. We aimed to investigate a possible association between available income as a proxy for SEP and development of IE in a nationwide Danish cohort.

Materials and methods

Study population

All permanent residents in Denmark are assigned a unique and permanent Civil Personal Registration (CPR) number at birth or immigration, which is used during every contact with the Danish health care system. The Danish nationwide administrative registers hold information on hospitalizations with diagnosis codes (ICD-10) and procedural codes, redeemed prescriptions from pharmacies, demographic information, income- and vital status. All registers can be cross-linked through encrypted CPR numbers, allowing for nationwide data on several parameters.[17,18]

We identified all Danish residents between 30 and 80 years of age in the time period from January 1, 2007, to December 31, 2017 from the *Danish Civil Registration System.*[17,18] Information on date of birth and death, sex, and demographics (country of origin and immigration/emigration dates) was obtained. We excluded first generation immigrants, patients with IE prior to inclusion and patients with missing data related to income (Figure 1). The final cohort comprised individuals between 30 and 80 years of age, who resided in Denmark during the study period and had all the necessary information on SEP. Baseline characteristics were assessed at the time of study entry (January 1, 2007 or date of 30st birthday if in the study period but later than start of study). The cohort was divided into quintiles based on income and followed until the first of the following events: a first episode of IE, emigration, death, or end of study period (December 31, 2017).

Income as a proxy for socioeconomic position

Socioeconomic position is a complicated and multifaceted concept which can be evaluated from different angles and with different approaches. Patients diagnosed with IE are often of older age and studies have previously found income and wealth to be influential socioeconomic risk factors in elderly individuals.[19,20] Therefore, adjusted disposable income was used as an indicator of SEP, as applied in previous studies.[21-23] The income-data was extracted from *The Income Statistics register* provided by statistics Denmark[24] and linked to health care data by encrypted CPR-numbers. The disposable income was centrally calculated by Statistics Denmark and represents the available disposable income of a household (personal income from: salaries, social transfers and benefits, private pensions, imputed rent of privately owned property, and income from savings and investments [eg, interest and share return] after deduction of taxes and negative interest)[25,26] corrected according to OECD's modified equivalence scale[27] (The first adult counts as 1, additional adults as 0.5 and children < 14 years counts as 0.3). The variable is registered yearly and was manually corrected for inflation until 2015. To account for yearly variation in income, an average of disposable income 5 years prior to baseline was divided into quintiles and used to define 5 levels of SEP. Information on disposable income was extracted throughout the study period and updated time-dependently every year, making it possible to change level of SEP continuously (Supplementary Table 1).

Comorbidities and outcome

Data on outcome, comorbidities and invasive procedures were obtained from *The Danish National Patient Register* which contains dates and discharge diagnoses for all hospital admissions in Denmark since 1977.[18] Data on comorbidities mainly diagnosed or treated outside the hospital were extracted from *The National Prescription Registry* which contains information on amount and date of dispensing for all claimed prescriptions since 1994, using the Anatomical Therapeutic Classification (ATC) as identifier.[28,29] As previously applied, patients with cyanotic congenital heart disease or prosthetic heart valves were considered at high risk of developing IE,[10] while patients with cardiac implantable electronic devices, acquired heart valve disorder or hypertrophic cardiomyopathy were considered at moderate risk of IE.[11]

Data on vital status was extracted from the Danish Civil Registration System.[17,18] The individual comorbidities and definitions hereof are listed in the Supplementary Table 1.

The primary outcome was defined as a first episode of IE, defined as a hospital admission with diagnoses codes for IE (ICD-8: 421; ICD-10: DI33, DI38, DI398) and an admission length of ≥ 2 weeks, or death within the first 2 weeks of an IE admission (Supplementary Table 1). The diagnosis of IE has previously been defined and validated with a positive predictive value of 90%.[30] Every individual with an admission that fulfilled the same IE criteria prior to the inclusion date was excluded. The date of

Figure 1. Title: Flowchart. Legend: Flowchart of the study cohort obtained from nationwide registers. Abbreviations: IE, Infective endocarditis.
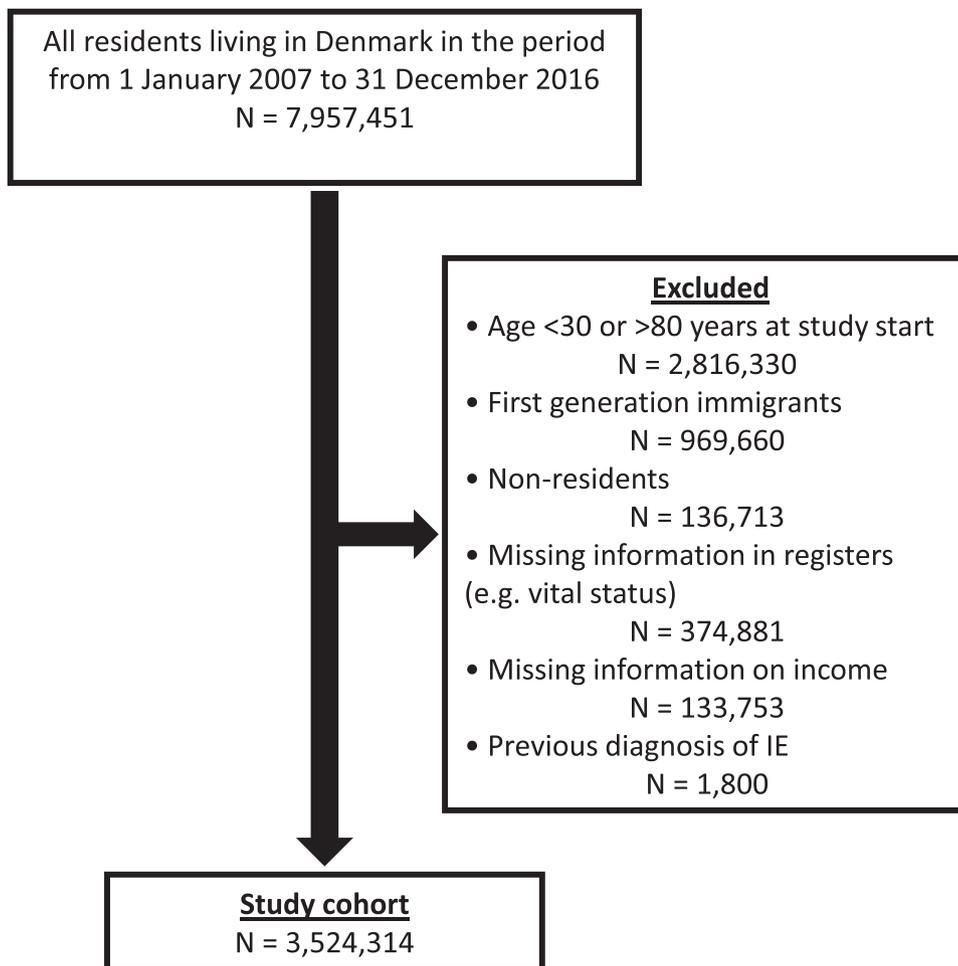
first episode of IE was defined as the admission date of the hospitalization.

Statistical analysis

Categorical variables are presented as frequencies and percentages and data were compared using chi-squared test. Continuous variables are presented as medians with interquartile ranges (IQR) and data were compared using the Student's t-test. A 2-sided P-value $< .05$ was considered statistically significant.

Poisson Regression analyses were used to investigate the association between SEP and first episode of IE. Events of IE were reported as incidence rate ratios (IRR) with 95% confidence intervals (CI). The analyses included 2 timescales: (1) calendar time and (2) age, both in 5-year time-bands after January 1, 2007 and the 30 birth date, respectively. Prespecified adjustment variables included time dependent age and calendar time, sex and chronic comorbidities at baseline (heart valve disease, congestive heart failure, congen-

ital and rheumatic heart disease, Human Immunodeficiency Virus (HIV), diabetes, liver disease, chronic renal failure, chronic obstructive pulmonary disease, renal dialysis, and implanted prosthetic devices). Interaction with sex and age was investigated and analyses were stratified accordingly. Statistical calculations were performed using SAS for Windows, version 9.4 (SAS Institute Inc., Cary, NC, USA) and R Core Team (2023). _R: A Language and Environment for Statistical Computing_. R Foundation for Statistical Computing, Vienna, Austria. <https://www.R-project.org/>.

Ethics approval

In Denmark, no ethics approval or informed consent is needed for retrospective register studies. All data are held by Statistics Denmark and permission to use data from the Danish national registries has been granted by the Knowledge Center on Data Protection Compliance – The Capital Region of Denmark (approval number: P-2019-382).

Table 1. Clinical characteristics at baseline stratified by income quintiles

	Annual income in quintiles					
	1 (lowest)	2	3	4	5 (highest)	Total
N (%)	704,865 (20.0)	704,865 (20.0)	704,860 (20.0)	704,864 (20.0)	704,860 (20.0)	3,524,314
Age, median (IQR)	46.1 (30.3-69.2)‡	43.4 (32.6-61.1)‡	43.0 (33.2-55.7)‡	47.0 (35.9-57.5)‡	54.4 (44.4-60.6)	47.3 (34.8-60.5)
Male (%)	334,576 (47.5)‡	336,052 (47.7)‡	357,814 (50.8)‡	359,990 (51.1)	360,117 (51.1)	1,748,549 (49.6)
Full follow-up (%)	399,475 (56.7)‡	493,614 (70.0)‡	532,542 (75.6)‡	564,435 (80.1)‡	614,431 (87.2)	2,604,497 (73.9)
Comorbidities (%)						
Heart valve disease	6,370 (0.90)‡	4,290 (0.61)‡	3,050 (0.43)‡	2,869 (0.41)‡	3,368 (0.48)	19,947 (0.57)
Heart failure	12,126 (1.72)‡	7,162 (1.02)‡	4,101 (0.58)‡	3,317 (0.47)‡	3,492 (0.50)	30,198 (0.86)
Congenital heart disease	3,284 (0.47)‡	3,200 (0.45)‡	2,740 (0.39)‡	2,201 (0.31)‡	1,437 (0.20)	12,862 (0.36)
Rheumatic heart disease	672 (0.10)‡	508 (0.07)‡	342 (0.05)	277 (0.04)‡	329 (0.05)	2,128 (0.06)
Diabetes	33,640 (4.77)‡	25,605 (3.63)‡	18,473 (2.62)‡	16,949 (2.40)	17,005 (2.41)	111,672 (3.17)
HIV	750 (0.11)‡	518 (0.07)‡	398 (0.06)	348 (0.05)	377 (0.05)	2,391 (0.07)
Liver disease	4,142 (0.59)‡	3,020 (0.43)‡	2,005 (0.28)‡	1,792 (0.25)‡	1,649 (0.23)	12,608 (0.36)
Chronical renal failure	375 (0.05)‡	427 (0.06)‡	377 (0.05)‡	341 (0.05)	320 (0.05)	1,840 (0.05)
Renal disease	554 (0.08)‡	566 (0.08)‡	510 (0.07)‡	436 (0.06)	422 (0.06)	2,488 (0.07)
COPD	113,781 (16.1)‡	99,338 (14.1)‡	85,031 (12.1)‡	79,632 (11.3)‡	77,458 (11.0)	455,240 (12.9)
Cancer	20,652 (2.93)‡	16,896 (2.40)‡	13,631 (1.93)‡	14,467 (2.05)‡	19,530 (2.77)	85,176 (2.42)
Atopic dermatitis	592 (0.08)‡	562 (0.08)‡	484 (0.07)‡	495 (0.07)‡	392 (0.06)	2,525 (0.07)
Rheumatic disease	5,777 (0.82)‡	5,017 (0.71)‡	3,835 (0.54)	3,589 (0.51)‡	3,936(0.56)	22,154 (0.63)
Chronic dialysis	908 (0.13)‡	783 (0.11)‡	473 (0.07)‡	440 (0.06)	403 (0.06)	3,007 (0.09)
Invasive procedure*	81,777 (11.6)‡	82,486 (11.7)‡	78,512 (11.1)‡	76,573 (10.9)‡	69,657 (9.88)	389,005 (11.0)
Prosthetic device† (%)						
Major cardiac device	5,259 (0.75)‡	3,636 (0.52)‡	2,610 (0.37)‡	2,419 (0.34)‡	2,895 (0.41)	16,819 (0.48)
Extracardiac device	54,215 (7.69)‡	43,814 (6.22)‡	34,333 (5.10)	36,462 (4.87)‡	36,014 (5.17)	204,773 (5.81)

Quintiles of income are based on a 5-year average of annual income prior to index.
Abbreviations: COPD, chronic obstructive pulmonary disease; HIV, human immunodeficiency virus; IQR, interquartile range.
 * Any surgical procedure within 1 year prior to study inclusion.
 † Prosthetic devices implanted at any time prior to index; Major cardiac device: Pacemaker and implantable cardioverter defibrillator, prosthetic valves, clips and rings not including cardiac stents.
 ‡ Significant values (*P* < .05) compared to the highest income quintile.

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Results

A total of 3,524,314 individuals were included in the study cohort (Figure 1) and followed for a median of 11.0 years (IQR = [10.1; 11.0]). 73.9% of the cohort achieved a full follow-up. Clinical characteristics at baseline, stratified by income quintiles, are presented in Table 1. The median age at inclusion was 47.3 years (IQR = [34.8; 60.5]) and men and women were equally distributed through the income quintiles. Individuals with the lowest income were more often female, had more chronic comorbidities and implantable devices compared to individuals with the highest income. Furthermore, a range of comorbidities including heart valvular disease, heart failure and congenital heart disease, as well as invasive procedures and implantation of prosthetic devices were less frequently observed in the high-income group.

Rates of infective endocarditis

Of the 3,524,314 individuals included in the study cohort, a total of 3,935 individuals (0.11%) were diagnosed with a first episode of IE during the study period. Patients who were diagnosed with IE during the study were predominantly male (69.5%) and had a median age of 70.5 years (IQR = [61.6; 77.8]) at the time of IE diagnosis. High risk comorbidities (cyanotic congenital heart disease or prosthetic heart valves) were present in 22.7% of the patients, while 50.9% had a moderate risk comorbidity (cardiac implantable electronic devices, acquired heart valve disorder or hypertrophic cardiomyopathy) (Supplementary Table 2).

A significant trend with increasing incidence of IE by decreasing income level was observed with incidence rates (IR) ranging from 7.39 to 20.36/100,000 person-years (Figure 2). Correspondingly, after adjustment we observed a significantly higher IRR = 1.58 [95% CI 1.43-1.75] in the lowest income level compared to the highest income level (Figure 2).

The association between income and IE differed by age (*P* for interaction <.001) but not with sex (*P* = .33). After stratification the IR of IE increased with high age and low income, with rates ranging from 23.7 to 32.9/100,000 person-years across income groups in patients ≥65 years old and from 1.2 to 6.1/100,000 person-years in the patients aged 30-44 years (Figure 3). The association between IE and disposable income was consistent through all age groups but was most pronounced for the younger

Figure 2. Title: Incidence rate and ratios for infective endocarditis. Legend: Incidence rates for each income quintile, unadjusted incidence rate ratios (IRR) and a fully adjusted model of IRR for first episode of infective endocarditis according to time-dependently updated income quintiles. The full model is adjusted for age, sex, 2 periods of 5 calendar years, heart valve disease, congestive heart failure, congenital and rheumatic heart disease, HIV, diabetes, liver disease, chronic renal failure, chronic obstructive pulmonary disease, renal dialysis, and implanted prosthetic devices. Highest income quintile as reference.

Socioeconomic position	Incidence rate /100,000 person-years	Events	Unadjusted IRR (95% CI)	Adjusted IRR (95% CI)	Forest plot
1 - lowest	20.36	1,108	2.76 (2.51-3.02)	1.58 (1.43-1.75)	
2	16.95	987	2.29 (2.09-2.52)	1.45 (1.31-1.60)	
3	10.54	574	1.43 (1.28-1.59)	1.28 (1.15-1.43)	
4	7.74	506	1.05 (0.94-1.17)	1.10 (0.98-1.23)	
5 - highest	7.39	760	Reference	Reference	

Figure 3. Title: Incidence rate and ratios for infective endocarditis stratified by age group. Legend: Incidence rates for each income quintile and a fully adjusted model of incidence rate ratios for first episode of infective endocarditis according to time-dependently updated income quintiles, stratified by age groups (30-44 years of age, 45-64 years of age, and ≥65 years of age). The model is adjusted for age, sex, 2 periods of 5 calendar years, heart valve disease, congestive heart failure, congenital and rheumatic heart disease, HIV, diabetes, liver disease, chronic renal failure, chronic obstructive pulmonary disease, renal dialysis, and implanted prosthetic devices. Highest income quintile as reference.

Socioeconomic position	Incidence rate/ 100,000 person-years	Events	Forest plot	Incidence rate ratio (95% CI)
Age 30-44				
1 - lowest	6.11	93		5.09 (3.38-7.69)
2	2.87	48		2.48 (1.57-3.91)
3	1.96	40		1.67 (1.04-2.67)
4	1.28	30		1.07 (0.65-1.78)
5 - highest	1.22	30		Reference
Age 45-64				
1 - lowest	13.06	181		2.52 (2.10-3.02)
2	10.16	181		1.97 (1.64-2.36)
3	8.34	174		1.64 (1.37-1.98)
4	6.89	212		1.37 (1.15-1.63)
5 - highest	5.05	317		Reference
Age 65+				
1 - lowest	32.92	834		1.26 (1.11-1.42)
2	31.97	758		1.19 (1.05-1.34)
3	27.38	360		1.02 (0.88-1.17)
4	23.68	264		0.88 (0.76-1.03)
5 - highest	26.58	413		Reference

age groups. Eleven-year cumulative incidence curves of IE stratified by income level and age group are available online (Supplementary Figure 1A-C).

Discussion

In this nationwide cohort study, including more than 3.5 million Danish residents, we examined the association between disposable income as a proxy for SEP and IE through the years 2007 to 2017. The main finding from our study was a significant association between income and the occurrence of IE. We found that the incidence of IE increased with decreasing income and observed a higher incidence rate of IE among residents aged ≥65 years compared to residents aged 45-64 and 30-44 years, respectively. After adjustment, the IRR of IE was higher in the low-income quintiles compared to the highest quintile. This observation persisted through all age groups but was most pronounced for the younger individuals.

Income and socioeconomic position as a risk factor for infective endocarditis

Risk factors for IE have historically been assessed from somatic diseases and conditions and from objective findings as highlighted by the 2023 European Society of Cardiology modified diagnostic criteria of infective endocarditis.[1] High- and intermediate risk conditions for IE include the presence of prosthetic heart valves, previous IE, and congenital- and structural heart disease, while major diagnostic criteria include specific findings from imaging and microbiology to verify the IE diagnosis.

Our findings suggest income as a proxy for SEP to be an important factor to consider when assessing the risk of IE. The association between low SEP and increased risk of infections in general has been established in previous studies. Wang et al. used the REGARDS cohort to demonstrate an association between increased risk of sepsis and low SEP assessed by both income and educational level.[31] Tong et al. observed a higher incidence of *Staphylococcus aureus* bacteraemia (SAB) among patients with low SEP compared to patients with high SEP in a prospective cohort of Australian and New Zealand patients.[32] In Danish data, Østergaard et al. observed low SEP to be associated with an increased risk of SAB but were unable to establish a significant association between SEP and IE subsequent to SAB (IRR 1.20 [95% CI 0.79-1.81]).[15] This latter discrepancy compared to our results may reflects multiple aspects: We defined SEP according to disposable income because of a previously shown association between available income and health outcomes in old age[19] while Østergaard et al. used highest attained educational level. All levels of education in Denmark, from primary school through university, are free of charge for Danish residents, which could diminish the impact of education as a proxy of SEP. Additionally, it is important to notice that the IE populations differ between the studies, given that only patients with IE secondary to SAB was included in the study by Østergaard et al. *Staphylococcus aureus* has been observed as the main microbiological pathogen in 28%-43% of IE cases in Europe and North America[3] and thus the population included by Østergaard et al. is selected compared to ours, which include all IE patients regardless of microbiologic origin. This is also reflected in the number of IE patients included the 2 studies (776 vs 3,935 IE patients).

Study population

When comparing clinical characteristics at baseline in the income quintiles used to stratify our study population, we observed that the high-income group were older and more frequently of male sex compared to the lower income groups. Additionally, a range of chronic comorbidities including valvular disease, congestive heart failure, HIV, renal dialysis, surgical procedures within 1 year prior to IE diagnosis and implanted foreign bodies were more frequently encountered in the lower income groups compared to the highest income group. Several of these factors are known risk factors for IE,[1] and might contribute to the increased risk of IE observed in the lower income groups. However, the association between income and IE persisted after statistical adjustment for these same factors suggesting that low income as a proxy for low SEP by itself contributes to an increased risk of IE. While we adjusted for known confounders it is important to consider the risk of reverse causality. Serious acute and chronic disease might affect the ability to perform and maintain work force attachment and thereby affect income level which in turn would lead to a downward shift in SEP level. This mechanism may complicate the interpretation of income as a proxy for SEP as an independent risk factor. By using adjusted disposable income and starting inclusion by age 30 we aimed to account for this uncertainty. The analysis stratified by age showed a consistent pattern of increasing incidence of IE by decreasing income through all age groups, but less pronounced in patients aged 65 or more. This observation suggests that chronic comorbidities and frailty of the elderly, in addition to competing risk of death, probably has more impact in older patients compared to the younger ones in relation to risk of IE, although SEP may play an additional role.

Health outcomes and socioeconomic position

The observed association between low disposable income and IE might be explained by several aspects. It is unlikely that little financial leeway in itself is responsible for the increased risk of IE, but low disposable income, and thereby low SEP, might be tied to poor health awareness, selfcare, and health literacy, factors that could increase the risk of delayed healthcare contact and diagnosis and decreased quality of treatment. Additionally, low SEP might be associated with social determinants of poor health eg, exposed and risky jobs, risky lifestyle in general with possible drug abuse, and social isolation and thus consequently inadequate contact to healthcare systems. Furthermore, cultural and linguistic barriers could also contribute to a poor understanding of and contact to the healthcare system with poor health as the ultimate consequence. All factors which could increase the risk of infections in general. A link between low SEP and decreased ability to cope with life changing events and stress management has previously been demonstrated.[33] All of the abovementioned factors might contribute to the observed differentiated risk across SEP levels.

An association between lower SEP and worse health outcomes following IE has been shown previously. In a prospective cohort of 3,113 IE patients across 40 countries, Sengupta and colleagues observed that low-income patients compared to high-income patients had later clinical presentation [median (IQR) days since symptom onset: 31 (12-62) vs 12 (3-35)], less frequent use of surgery in patients with an operation indication (51.3% vs 75.5%)

and increased mortality (23.7% vs 15.0%).[34] Strobel et al. examined the association between SEP defined as Distressed Communities Index (DCI) and various health outcomes following IE-related valve surgery.[35] They observed an association between high DCI (low SEP) and increased operative mortality, major morbidity (deep sternal wound infection, reoperation for any reason, permanent stroke, prolonged ventilation, or renal failure) and increased length of hospital stay, respectively. Additionally, Butt et al. showed that a high level of education compared to basic school [OR 5.47, 95% CI 2.05-14.6] and high income compared to low income [OR 3.17, 1.85-5.46] were associated with higher odds of a return-to-work-force attachment 1 year after IE diagnosis.[36]

These observations on SEP and IE in combination with our findings highlights that patients with low SEP seems to be more prone to develop IE and subsequently experience a more serious course of disease with associated worse outcome compared to patients with higher SEP. Socioeconomic inequality has previously been observed for a variety of diagnoses.[37-39] Our results suggest that socioeconomic inequality also exists with respect to IE and underscores the need for attention and observance with respect to prevention, early detection and diagnosis, treatment initiation, continuous treatment adjustments and appropriate rehabilitation in order to help equalise this observed inequality in healthcare.

We conducted our study in a Danish cohort in which all patients had equal and free access to examination, tests, and treatment in the public healthcare system, thus minimizing social inequality.[40] Despite this we observed a skewed socioeconomic burden of IE. One can only speculate if the magnitude of inequality had been an even bigger in a society with healthcare dependent on private funds or insurance coverage. Additionally, one would expect an increased socioeconomic gradient in developing countries where the availability of and access to specialized healthcare might be limited, thus highlighting the disparities in a global perspective. It has previously been demonstrated that low SEP is tied to limited health care access and resulting poor health.[41] This observation in conjugation with the increased risk of IE and worse outcome following IE emphasizes the need for differentiated efforts across SEP-levels in an attempt to relevel the observed inequality. Our results combined with the previously observed poorer prognosis among patients with low SEP levels raises the question of whether SEP needs to be accounted for when evaluating the IE risk in a patient. SEP is not applicable on a single patient level but might be considered on a population-based level for the purpose of prevention of IE.

Disposable income as a proxy for socioeconomic position

We used disposable income to define SEP given that wealth and income previously have been shown as important socioeconomic factors in elderly individuals[19,20] and in line with previous studies.[21-23] To account for the inherent challenges with low income in young age and after the age of retirement, we chose to start inclusion at age 30, given that most individuals are expected to have finished education at this age and thereby to have a somewhat stable income. Furthermore, we used a corrected measure of disposable income (see methods section) which accounts for active and passive wealth, social transfers and benefits and imputed rent of privately owned property which in turn should provide a fairer perspective of income after retirement.

Strengths and limitations

The present study has several important strengths. It includes the completeness of data in this nationwide unselected cohort of Danish residents, ensuring a minimal loss to follow-up. Furthermore, the risk of selection bias is limited by including the entire Danish population. We did however exclude first-generation immigrants due to non-available health information prior to immigration eg, congenital heart disease, prior IE, prior valvular or vascular implants etc. which potentially could introduce selection bias in the context of socioeconomic disparities among immigrants. The definition of IE in the registers has previously been validated which optimizes the chance of finding true events in the cohort.[30] In addition, the register-based study design allowed for complete and accurate information on income in the cohort, which might be a challenge in studies including questionnaires, were individuals can be reluctant to provide such information.[42] To account for the possibility of individuals changing income and thereby SEP status throughout the study period, the interchangeability of income[42] was used by updating the measure time-dependently every year.

The observational design of the study does not allow for causal interpretations as only associations can be demonstrated. Further limitations of the study are possible inadequate information on risk factors for developing IE, due to the register-based study design with a risk of these were not reported systematically. These risk factors count dental procedures (which is paid by the individual citizen with a small amount being reimbursed by the public health care system),[1] intravenous drug use, lifestyle including smoking and alcohol consumption and comorbidities that was treated nonpharmacologically or solely by a practitioner (eg, diet-treated diabetes). To accommodate the challenge of possible inadequate information of injection drug use, which is a known major IE risk factor,[43] individuals with a preceding diagnosis of IE were excluded and adjusted for comorbidities that heightens the risk for IE among intravenous drug users (ie, HIV[44]).

Another limitation is disposable income which can be influenced by reverse causality, where income markedly

decreases based on eg, health status. Furthermore, the subject is not strait forward and there is a risk of confounding and mediator effects from several sides. Congenital heart disease is a known risk factor for IE, specifically in young age, and might at the same time affect the work capacity and thereby income level of the affected individual. In an attempt to overcome this issue, we only included individuals from 30 years of age. Other chronic diseases and conditions eg, I.V. drug abuse and heart disease leading to implantation of prosthetic material might also affect the life course and income opportunities of affected patients, while at the same time being independent risk factors for IE.

Conclusion

In this nation-covering cohort study we found a significant inverse relationship between disposable income as a proxy for socioeconomic position and development of infective endocarditis. While the absolute risk of infective endocarditis is highest among older individuals, the association between low disposable income and infective endocarditis was strongest in younger age. These findings underscore the need for differentiated health efforts across socioeconomic positions to prevent and relevel inequality in health.

Conflict of interest

All authors declare that they have no known conflicts of interest.

CRediT authorship contribution statement

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Data availability statement

Access to the registries contained within the facilities hosted by Statistics Denmark is granted on individual basis by the relevant authorities. For this reason, the underlying data for this study are not publicly available.

Declaration of generative AI and AI-assisted technologies in the writing process

No generative AI or AI-assisted technologies were used in the preparation of this manuscript.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ahj.2025.04.003.

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