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Review

The economic burden of Tuberculosis in Denmark 1998-2010. Cost analysis in patients and their spouses

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ABSTRACT

Objective: To evaluate the economic burden of tuberculosis (TB) in Denmark,
Methods: 8,433 Danish TB-patients (1998-2010) were matched with 33,707 controls by age, gender, civil status and geography. Health-related costs (health system contacts and –procedures, medications) and socio-economic parameters (foregone earnings and social transfer expenses) were calculated on data from national databases. The same information was obtained for 3,485 spouses of TB-patients, and 17,403 controls.
Results: Health-related costs were higher for cases throughout the period. Before diagnosis, cases posed € 1,180 more health costs per year than controls. Excess health costs in the 2 years around diagnosing and treating TB were € 10,509. Cases received an average excess public transfer income of € 3,345 before vs. € 3,121 after diagnosis. Average employment income deficiency was € 11,635 before vs. € 13,885 after diagnosis, but the increasing difference showed a linear shape throughout the period. Spouses also had lower income, more social transfer, and posed higher health-related costs than matched controls.
Conclusion: We estimate the direct costs per TB patient to be €10,509. TB patients and their households are characterized by increasingly lower employment income, lower employment rate, and higher dependency on public transfer, but the socio/economic deterioration is rather a risk factor for TB than a direct consequence of the disease.

1. Introduction

Worldwide, tuberculosis (TB) remains the deadliest of contagious diseases with almost 9 million new cases and 1.3 million deaths in 2012.[1] Previous studies of the economic burden of TB have mainly focused on direct costs related to hospitalisation and treatment of TB,[2–4] though Miller et al.,[5] found that direct treatment-related expenses accounted for only a minor part of the $ 376,255 total costs for society per TB case. In a European context, Diel et al.,[6] calculated the direct costs of diagnosing and treating a case of pulmonary TB to be € 16,389, and indirect costs to be € 2,461, in 2004. In 2009, the sum of direct and indirect costs had decreased to € 11,239 per adult case (excluding MDR-TB)[7]; close to the €10,282 average in Western Europe according to a 2013 review.[8] The decrease in costs reflects increasing out-patient treatment of TB. Incorporating indirect costs of TB has previously been based on estimated loss in productivity as factual data have generally not been available.

Denmark has a low TB incidence (2012: 6.5 per 100.000 per year).[9] About 66% of TB cases are found among immigrants. The responsibility for treatment and follow-up of TB patients is shared among centralized departments of pulmonary and infectious diseases, while contact investigation procedures are performed at a handful of public departments of respiratory diseases. Guidelines for TB treatment and contact investigations are defined in the national Danish TB-program.[10] In contrast to comparable countries,

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the TB incidence in Denmark has not declined in recent years, primarily due to active disease transmission in high risk subpopulations.[11] In Denmark, data on healthcare contacts, medication use, employment information, and social determinants at the person level are linked by the unique civil registration number. This allows reliable calculation of direct and indirect costs of a given disease, and has previously contributed important knowledge of the financial burden of a number of chronic diseases.[12–14]

To our knowledge, no previous studies have evaluated the impact of diagnosing and treating TB on social and economic parameters over time, nor have they addressed the socioeconomic status of spouses of TB patients. The aim of this study was to evaluate health-related costs and socio-economic parameters of patients with active TB and their spouses both before and after diagnosis and treatment in a national, retrospective case-control study.

2. Methods

In Denmark, all hospital contacts are registered in the National Patient Registry (NPR).[15] The NPR includes administrative information, primary and secondary diagnoses and information on diagnostic and treatment procedures using the International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10). Primary sector contacts (general practice and specialist care) and the use of medications are recorded in the databases of the National Health Security and the Danish Health and Medicines Agency, respectively.

We extracted data on all patients with a primary or secondary ICD-10 diagnosis of A15 through A19 in the period 1998-2010 (12 years). This includes pulmonary and extra pulmonary TB, but not latent TB (LTBI). We did not control for MDR-TB status, as the incidence in Denmark is very low (2011: 0.48% of TB cases[9]). Data were available for the entire observation period, allowing us to trace patients both retrospectively and prospectively relative to the time of diagnosis.

The Danish Civil Registration System contains information about cohabitation status, marital status, social factors, employment, education, income, pensions etc.[16]. We randomly selected controls matched by age, gender, geographical area and marital status. Patient-to-control ratio was 1:4.

Data from patients and matched controls that could not be identified in the Income Statistics database were excluded, but more than 99% of the observations were successfully matched. If a patient or control was not present in the registry on 1 January in a given year because of death, imprisonment or emigration, the corresponding control or case was excluded.

Spouses were identified by having the same address as a case or by marital status. The random control group for spouses was generated similarly to the control group for TB patients.

Patients, spouses and matched controls were followed through the study period from 1998 to 2010 (or until death). If diagnosis of TB was made in 1998, we were able to follow that individual 11 years forward in time. If the diagnosis was established in 2010, we were able to trace that individual 11 years backwards in time. If the diagnosis was made in 2006, we could trace eight years backwards and four years forward etc. This allowed us to study changes in health costs and socio-economic parameters relative to the TB diagnosis reflecting the impact of TB on these parameters, while baseline differences between cases and controls allowed us to study fundamental socio-economic differences between cases and controls (risk factors for TB).

Health-related costs covered in- and out-patient treatment and medicine expenditures. Average national costs of hospitalisation and outpatient treatment for specific diagnosis-related groups (DRG) were calculated. These data were obtained from Danish Ministry of Health by DRG. It is average *case-mix* of in- and out-patient costs, updated for every year. Specific patient-related outpatient costs were added. Medicine expenditures were obtained from the Danish Health and Medicines Agency as the retail price of each drug (including dispensing costs) multiplied by the number of transactions. The frequencies and costs of consultations with general practitioners and other specialists were based on National Health Security data.

Socio-economic parameters included costs for society and patients, such as reduced employment benefits and social transfer payments. In Denmark, social transfer payments comprise subsistence allowances, pensions, social security, social assistance, publicly funded education support, and others. Indirect costs were based on income figures from Income Statistics. Costs were measured on an annual basis and adjusted to 2010 prices using Statistics Denmark's general price index. All costs were calculated in DKK and converted to Euros (€1: DKK 7.45).

2.1. Statistical analysis and ethical considerations

The study was approved by the Danish Data Protection Agency. Data handling did not involve revealing the identity of any patients or control subjects, so ethical approval was not required. Some patients had extremely high resource consumption, leading to a skewed distribution. From a societal perspective, this should be reflected in the results, and therefore, data were presented as means rather than as medians. Statistical analysis was performed using SAS 9.1.3 (SAS, Inc., Cary, NC, USA). Statistical significance of the cost estimates was established from two-sided t-tests based on bootstrap analysis.[17,18] A significance level of 0.05 was assumed for all tests.

3. Results

3.1. Demography

We identified and extracted 8,433 patients from the NPR, and 33,707 matched controls. Age, gender and educational level of the study population are shown in Table 1. We found more male (55.4%) than female (44.6%) patients, consistent with recent

Table 1
Distribution of age, gender and educational level among cases and controls

	Case		Control	
Age	N	%-Share	N	%-Share
<20	1,140	13.5	4,559	13.5
20-29	1,136	13.5	4,542	13.5
30-39	1,492	17.7	5,964	17.7
40-49	1,359	16.1	5,432	16.1
50-59	1,104	13.1	4,406	13.1
60-69	874	10.4	3,495	10.4
70-79	847	10	3,387	10
>=80	481	5.7	1,922	5.7
All	**8,433**	**100**	**33,707**	**100**
Gender	**N**	**%-Share**	**N**	**%-Share**
Male	4,668	55.4	18,655	55.3
Female	3,765	44.6	15,052	44.7
All	**8,433**	**100**	**33,707**	**100**
Education	**N**	**%-Share**	**N**	**%-Share**
Primary	3,197	37.9	10,438	31.0
Secondary	508	6.0	2,219	6.6
Vocational	1,598	18.9	9,253	27.5
Short college	235	2.8	1,280	3.8
Medium college	450	5.3	3,221	9.6
Master/phd	211	2.5	1,791	5.3
Unknown	2,234	26.5	5,505	16.3
All	**8,433**	**100.0**	**33,707**	**100**

Danish data.[19] An incidence peak was seen in the age group of 30-39 years. Generally, fewer cases had a college or university degree. The education levels were more often unknown for cases than for controls.

3.2. Health-related costs: Outpatient clinic, hospital, primary care and drugs

The health-related costs were significantly higher for cases than for controls in the entire study period (Figure 1 A), but as expected, the total health costs for cases showed a peak around the time of diagnosis. The mean case-to-control difference prior to diagnosis was € 1,180. Excess health-related costs in years 0-1 was € 10,509. The case-to-control difference levelled off from the second year after diagnosis, and mean case-to-control difference after the second year constituted € 1,322 per year. The largest health-related costs covered inpatient treatment; this was evident throughout the study period before as well as after diagnosis. In year 0-1, inpatient treatment constituted 76.6% of all health costs (81.3% in year 0 and 65.2% in year 1) (Figure 2). Health-related costs for both genders were higher for cases than controls in all age groups (Figure 3 A-B).

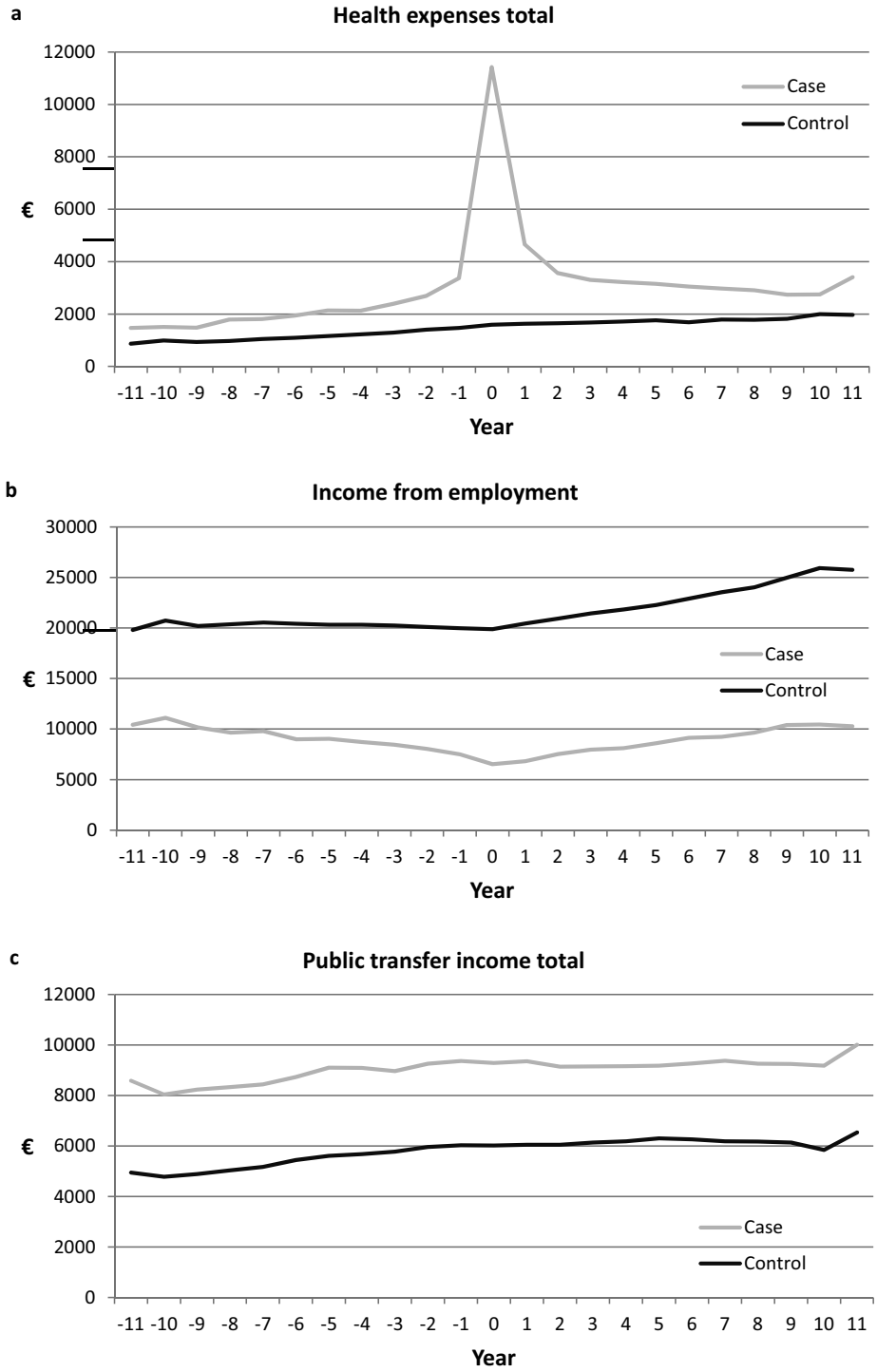

Figure 1. Total health expenses, cases and controls, relative to the year of diagnosis of TB.

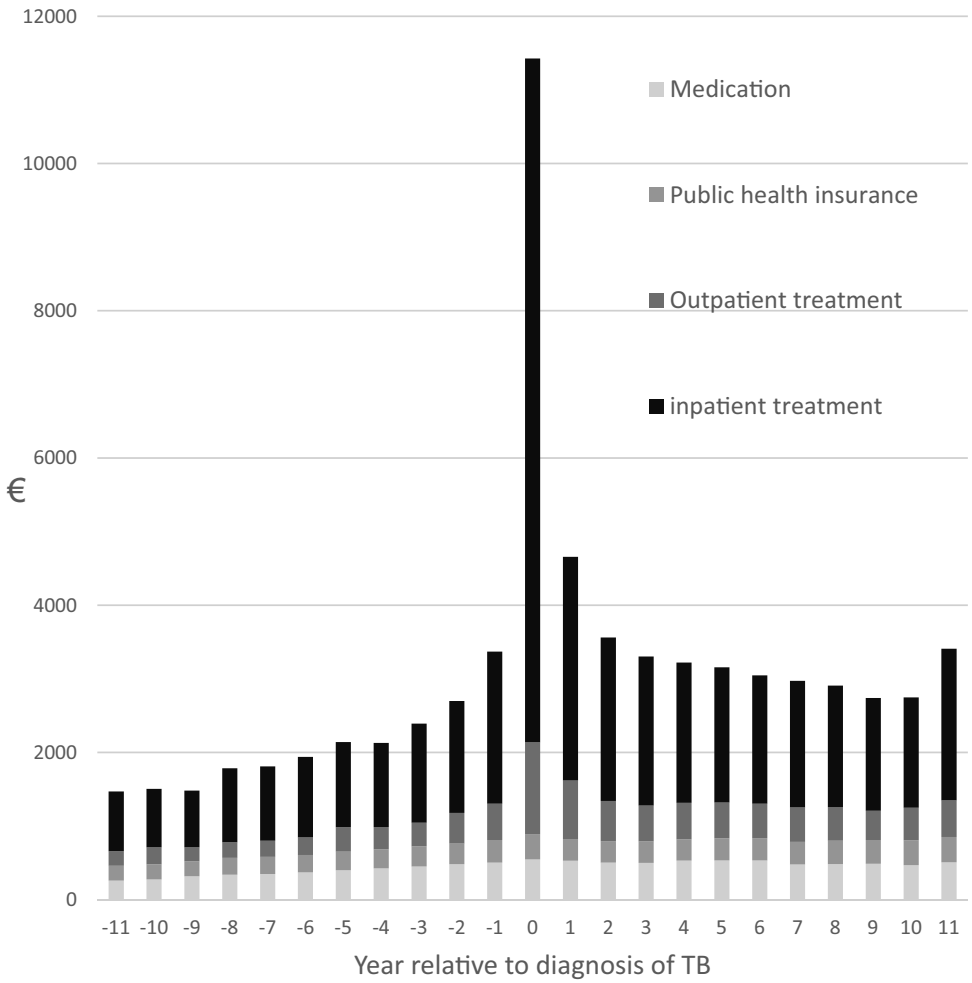

Figure 2. The contribution of different cost categories (inpatient treatment, outpatient treatment, public health insurance expenses and expenses to medication) to the total health costs for cases, relative to the year of TB diagnosis.

3.3. Socio-economic parameters: Foregone earnings, public transfer income, public pensions and sickness benefit

Throughout the study period, average employment income was lower for cases than controls; the opposite was true for social transfer income. (Figure 1 B-C) All differences between the groups regarding employment and social transfer income were statistically significant ($p<0.05$, data not shown). Average difference in employment income was € 11,635 in years prior to diagnosis, and € 13,885 after diagnosis. Average difference in total public transfer income was € 3,345 before diagnosis, and € 3,121 after diagnosis. However, changes in case-to-control difference regarding both employment income and public transfer income over time showed an approximately linear conformation (data not shown), and no major change in the trend was seen at the time of diagnosis.

Looking at employment and social transfer income distributed in age and gender groups (Figure 3), we found that income from employment was higher among controls in all age groups. For controls, social transfer income showed an increase at retirement age (a public pension is paid to all Danish citizens above 65 years when retiring). For cases, public transfer income was higher prior to retirement age, and increasing with age. The share of cases and controls receiving employment income and public transfer income is shown in Table 2.

3.4. Spouses of TB patients

3,485 spouses were included and matched to 17,403 controls. Being a spouse of a TB-patient was associated with increased social transfer income and lower employment income compared with controls (Figure 4 B-C). The difference was significant except in year 11, where few individuals contributed data (data not shown). The annual total health-related costs of spouses were higher than of controls (Figure 4 A), but only significantly in a period from four years before diagnosis to three years after diagnosis. The number of spouses and controls receiving employment income and public transfer income is shown in Table 2.

4. Discussion

Overall, we found that TB patients had higher health-related costs than matched controls long before the diagnosis of TB, and peaking at the time of diagnosing and treating the disease. Indirect costs for society as well as for the patients were higher for cases than for controls, up to 11 years prior to diagnosis. Of greatest importance was inferior employment income, which represents lost productivity for society as well as inferior income at individual level.

The education level data for cases and controls are generally robust for persons aged 14-80 years. For those above 80 years,

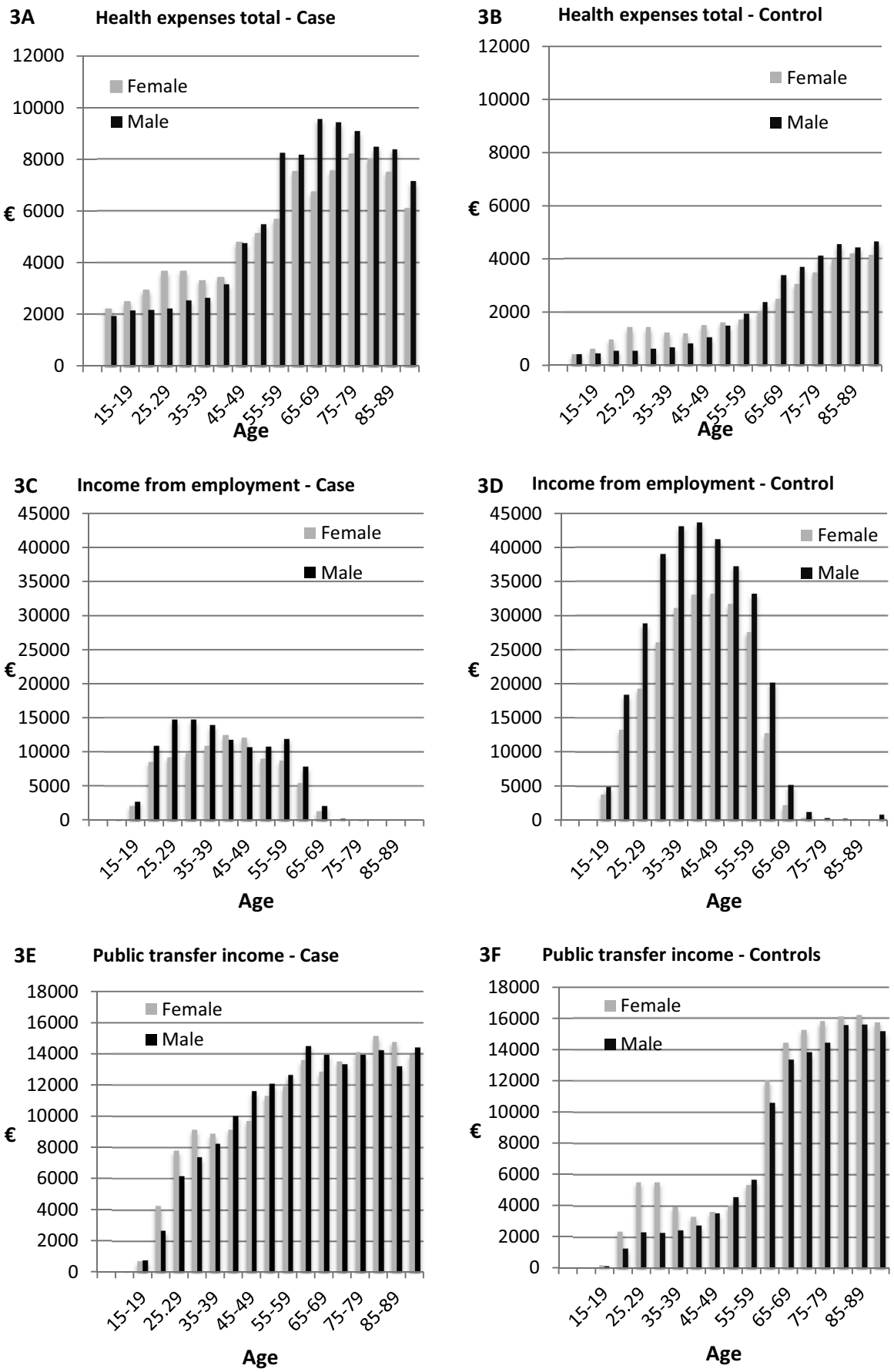

Figure 3. Expenses distributed for age and gender. Total health expenses for cases (3A) and controls (3B), employment income for cases (3C) and controls (3D) and public transfer income for cases (3E) and controls (3F).

Table 2
Share or cases and controls, and spouses and controls, receiving public transfer income. Person years after diagnosis of TB only. Some persons received more than one category of public transfer income in the included years.

		Cases			Spouses		
		Case	Control	P-value	Spouse	Control	P-value
Income from employment	%	31.3	58.5	<0.001	43.8	69.6	<0.001
Public transfer income total	%	68.3	47.3	<0.001	66.7	48.6	<0.001
Pension	%	*15.7*	*18.7*	<0.001	*15.7*	*14.9*	0.193
Other public transfers	%	*47.5*	*20.6*	<0.001	*44.3*	*21.9*	<0.001
Sickpay (public funded)	%	*9.8*	*12.0*	<0.001	*11.9*	*16.8*	<0.001

information is scarce, as registration from the different teaching institutions to the Danish Civil Registration System did not begin until 1970. This explains most of the controls with unknown education level, while unknown status was more common among cases. The majority of these probably had no education, many being immigrants from low-income countries, representing an important risk group for TB, not necessarily comparable to the controls with unknown status. In order to investigate the impact of educational level as a marker of socio-economic standing, we computed a general linear model (GLM), controlling for educational level including unknown status, to eliminate the effect of educational level. The significance level in case-to-control differences regarding health costs, income and social transfer did not change, except for health costs towards spouses in years 8, 9 and 10 after diagnosis, when few spouses and controls contributed data. The GLM illustrates that case-to-control

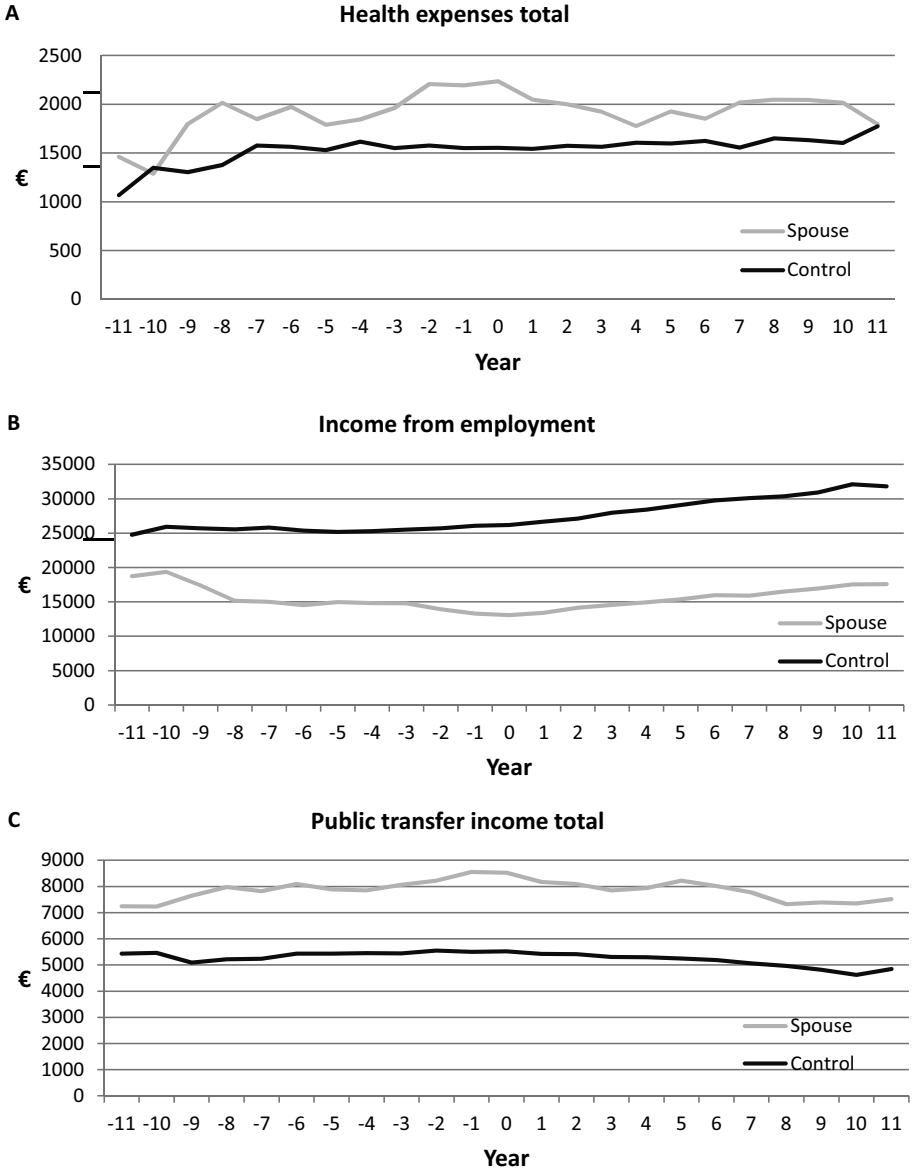

Figure 4. Spouses of TB-patients. Total health expenses for spouses and controls (4A), Employment income for spouses and controls (4B) and public transfer income for spouses and controls (4C), relative to the year of diagnosis of the TB-case.

differences could not be explained by different educational level, but it was not feasible for further analysis, as this would force us to exclude all cases and controls with unknown status, representing a clinically very important group of TB patients.

The total costs of diagnosing and treating a person with TB was approximately € 10,500, based on the excess costs in year 0 and 1, as we assume that these were attributable to TB. Standard TB treatment takes 6-9 months, though some cases require longer treatment. All economic data were registered per calendar year, whereby a large share of the expenses was denoted in year 1. Furthermore, the shape of the direct health-cost curve (Figure 1) supports that the excess health-related costs were concentrated in these two years. Spouses also posed higher health-related costs than matched controls, peaking around time of diagnosis, probably reflecting contact investigation, treatment for LTBI etc. Generally, around 30% of close contacts have LTBI,[20] often requiring investigation for active TB and treatment of LTBI.

A recent review estimated the direct costs per TB patient in Western Europe to be € 7,848 per drug-susceptible case,[8] which is close to the costs in Germany of €7,931 according to Diel et al.,[7] in 2009. These estimates were calculated on basis of number of hospital days, medicine expenditures, and outpatient costs specific for TB. The higher amount in our study may be explained by including total health costs, possibly including diseases leading to a risk of TB (e.g. COPD,[21] end-stage kidney disease,[22] diabetes mellitus[23],), but also the costs of secondary effects of TB and treatment such as difficult management of diabetes, deterioration in COPD, clinical depression treated in either primary or secondary sector etc . Average per-day costs of inpatient treatment have been estimated to be higher in Denmark compared with most other Western European countries.[24] Our data did not include costs related to contact investigation procedures; as such costs are not linked to the index TB patient but to the exposed contacts investigated. A prospective collection of data on contact investigation procedures would improve our knowledge of the economic aspects of this matter, and would need to take into account the estimated number of TB cases avoided and the reduced costs from TB cases identified at an earlier disease stage.

We found that persons developing TB as well as their spouses had lower employment income and higher dependency on public transfer income than matched controls. This was seen throughout the study period and also 11 years prior to diagnosis. Inferior employment income was the main contributor to these ‘‘indirect costs’’. They showed a linear shape over the years investigated, suggesting that the increasing income difference is a characteristic of the population group at risk of acquiring TB, rather than a direct consequence of TB disease. At the time of TB diagnosis, only 22.6% of TB cases vs. 54.5% of controls were gainfully employed. Taking these numbers into account, it is not surprising that the changes in income difference due to TB disease and treatment are small – simply because the majority of cases were unemployed already at the time of diagnosis. With regard to public transfer income, no major change was seen either before or after diagnosis or at the time of diagnosis for TB cases and their spouses. Therefore, the higher average public transfer income is also a characteristic of the population at risk of TB, rather than a consequence of TB disease.

In similar studies, indirect costs have been calculated from average sick leave. In comparison, we did not find a significant increase in case-to-control difference in income around the time of TB disease – probably because few TB patients were employed. In our point of view, the socio-economic deroute that constitutes a major risk factor for TB is of much greater societal importance, also economically speaking, than absence from work in the beginning of TB treatment. Diagnosing and treating TB requires close contact with healthcare professionals during several months. If this opportunity could be used to take precautions to prevent further deterioration, it would yield a potential for significant economic benefit for society as well as for patients.

The diagnosis and treatment of TB lead to major costs for society. The main part of health-related costs results from in-hospital treatment. Patients should only be admitted to hospital if they are severely ill, or if there is reason to believe that the patient cannot manage treatment in an out-patient setting. A strengthening of the out-patient management of patients, for example including TB consultations at home, in homeless shelters etc. could potentially reduce expensive in-patient treatments. However, earlier diagnosis of TB is probably the most effective way to reduce the need for hospitalisation of TB-patients, as well as to reduce overall costs due to complications and co-morbidities. TB is concentrated in certain high-risk communities in Denmark,[11] and screening for TB in these communities may be more cost-effective than contact investigation procedures.

There are some limitations to this study: Our findings depend on TB being diagnosed and reported correctly by clinicians. A previous study evaluated the NPR diagnoses of TB, and found a good positive predictive value (PPV).[25] The number of TB cases reported to the National TB Register (Statens Serum Insitut, Copenhagen) in the years investigated was 5,594,[26] and thus, the number of cases in this study was 33% higher. This may be due to underreporting of TB, to false-positive TB diagnoses or a combination. Previous studies in comparable countries have estimated underreporting of TB to be 7-27%,[27,28] while a study in Greece estimated an 80% underreporting.[29] Also, including spouses of TB patients implies certain concerns. Potentially, spouses of TB patients having active TB (being either infected by or being the source of infection of the case) could confound our findings. Yet, the risk of active TB in household contacts is around 1.4% in high-income countries,[20] and therefore, we assume that the effect of spouses having active TB would be minor. Finally, we did not provide background ethnicity data of either the study populations or the control groups, as we were not able to extract reliable ethnicity data from the registers used.

In conclusion, TB cases in Denmark are characterised by higher health-related costs than matched controls, also many years prior to TB diagnosis. The direct health-related costs peaked two years around diagnosis. Health-related costs per TB case were estimated to constitute approximately € 10,500. TB patients and their spouses are characterised by inferior employment and income, and higher dependency on social transfer income, compared with matched controls. These unfortunate socio-economic characteristics seemed to deteriorate over time and did not change significantly at the time of acquiring TB. TB in Denmark is connected to a pattern of socio/economic deroute, which in itself is much more dramatic than the indirect consequences of TB.

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Competing interests: None.

Ethics approval: The study was approved by the Danish Data Protection Agency.

Because data handling was anonymous, individual and ethical approval was not required.

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