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ORIGINAL ARTICLE

Healthcare and productivity cost of osteoporosis: a Danish register-based quasi-experimental study

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Abstract

Summary Osteoporosis significantly impacts healthcare costs in Denmark, with annual expenses exceeding €3097 per individual. The total annual burden of healthcare and productivity losses attributed to osteoporosis in Denmark surpasses €2 billion. Effective prevention, early detection, and management strategies should be considered to offset these costs and improve patient outcomes.

Purpose As the prevalence of osteoporosis rises, driven by an ageing population, quantifying its financial impact and guiding resource allocation becomes crucial. The aim of this paper is to establish the healthcare (medical and social care) costs and productivity costs attributable to osteoporosis and osteoporosis-related fractures in Denmark.

Methods The osteoporosis and osteoporosis fracture groups were identified from Danish healthcare registers using ICD-10 codes. The intervention group included individuals born in 1930–1950 with an osteoporosis diagnosis or an osteoporotic fracture with incidence between 2000 and 2021. A control group without osteoporosis and osteoporosis fractures was matched 1: 1 on a number of clinical and demographic variables from the general Danish population. Difference-in-difference approach was applied through generalised estimating equations with individual-level fixed effects to establish attributable costs.

Results Osteoporosis and osteoporosis-related fractures can be attributed with more than €3097 annually in healthcare costs for individuals aged 50 to 91, with expenses increasing sharply with age. Cumulative attributable healthcare (medical and social care) cost of osteoporosis between the ages of 50 and 91 was estimated at reach €127,000 per person. For the identified population of over 667,000 people with osteoporosis, the total annual healthcare burden attributable to the disease would amount to over €2 billion. The osteoporosis group also incurred an annual productivity loss of €3883, until the age of 66.

Conclusion Osteoporosis carries a pronounced economic burden for the health system and the individual. Resource allocative decisions should consider whether implementing strategies improving prevention, earlier detection, and better management of osteoporosis could be efficient given the high identified costs.

Keywords Osteoporosis · Danish registers · Healthcare and productivity cost · Register based study

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Introduction

Osteoporosis is a chronic progressive disease that is associated with low bone mineral density (BMD) resulting in weakened and fragile bones [1], which increases susceptibility to bone fractures [2].

Globally, all-age prevalence of osteoporosis has been reported as 23% in women and 12% in men, but with wide variation, with estimates for women ranging between 42 and 15.1%, for the African and American continents, respectively [3]. In Europe, the prevalence of osteoporosis is estimated at 19.8% for women and 9.7% for men [3], with prevalence increasing with age. Europe has seen the incidence of osteoporosis increase over the past decades [4], with osteoporosis-related fractures following a similar trend [5]. In Denmark, the incidence of osteoporosis-related fractures was estimated at 66,000 in 2010 [6], increasing to 86,000 in less than a decade, with most European countries observing a similar pattern [7]. Osteoporosis-related fractures have been associated with reduced quality of life and survival [8, 9], suggesting that an increase in incidence is likely to result in a larger burden associated with osteoporosis.

Osteoporosis also carries a substantial economic burden through direct healthcare costs, mostly attributable to fractures, and impact on productivity [6, 7]. Two studies estimated the total cost of incident fractures in Denmark: one estimated the costs at €1.45 billion in 2019, of which 850 million are attributed to direct costs of fractures [7] and another at €1.56 billion in 2013 [10].

However, the existing evidence of the economic burden of osteoporosis does not shed light on some important nuances. For example, it is not possible to differentiate whether the fractures occurred in people with an osteoporosis diagnosis, nor which part of the health system contributed to the costs (e.g., hospital, primary care, and medication) associated with osteoporosis. Furthermore, it is important to establish costs *attributable* to osteoporosis and osteoporotic fractures, as opposed to costs incurred for other reasons. This can be done by comparing groups with and without osteoporosis—an approach that has not been widely adopted in estimating costs associated with osteoporosis.

With an ageing population and an increasing prevalence of osteoporosis-related fractures, understanding the nuanced economic implications of this condition is essential for effective healthcare planning and resource allocation. Availability and reliability of Danish healthcare and administrative registers makes Denmark an ideal setting for a case-study on the economic cost of osteoporosis [11, 12]. The aim of this article was to establish the healthcare and productivity costs attributable to osteoporosis and osteoporosis-related fractures in Denmark.

Methods

A register-based quasi-experimental design was employed to estimate healthcare costs (defined as medical and health-related social care costs) and productivity costs attributable to osteoporosis in a cohort of people with osteoporosis and matched controls without osteoporosis.

Data

Study population

Administrative registers encompassing all individuals residing in Denmark were accessed through the Statistics Denmark Research Service. The study population was identified from the National Patient Register (NPR) and Danish National Prescription Register [13, 14]. The NPR captures all contacts with the hospital system in Denmark.

The osteoporosis group consisted of individuals born in 1930–1950 with an osteoporosis diagnosis or an osteoporotic fracture occurring between 2000 and 2021. The birth cohort and follow-up period were chosen to ensure a large enough sample of patients with osteoporosis was captured and was observed for sufficiently long, such that we had information on patients ranging in age from 50 until 89. The sample size of patients aged 90 + was too small to render statistically significant results (Supplementary Fig. 2). Osteoporosis diagnosis was defined as International Classification of Diseases, 10th edition (ICD-10) codes M80–M82 including primary and secondary diagnoses after the age of 50. An osteoporotic fracture was defined as hip fractures (ICD-10: S72, S72.0, and S72.1), vertebral fractures (ICD-10: M48.4, M48.5, M49.5, S22.0, S22.1, S32.0, S32.7, and S32.8), upper arm fracture (ICD-10: S42.2 and S42.3) and wrist fractures (ICD-10: S52.5, S52.6, S52, S52.5B, and S52.9) [10, 15, 16] including primary and secondary diagnoses. Further, individuals prescribed pharmaceuticals bisphosphonate (ATC-codes: M05BA01, M05BA04, M05BA06, M05BA07, M05BB01, M05BB03, and M05BA08 with more than nine months between prescriptions), strontium ranelate (ATC-code: M05BX03), denosumab (ATC-code: M05BX04) with more than five months between prescriptions, romosozumab (ATC-code: M05BX06), selective estrogen receptor modulator (SERM) (ATC-code: G03XC01), and parathyroid hormone analogue (ATC-code: H05AA02) [16, 17] were also included in the osteoporosis population. Hospital-based medical treatment with the following regiments also qualified individuals for inclusion in the osteoporosis group: with zoledronic acid (intravenous [IV] infusion) > 9 months between injections, or denosumab

(subcutaneous injection) (> 5 months between injections), or ibandronate (IV infusion) (> 3 months between injections) [18]. No explicit exclusion criteria were applied in this study. This approach was chosen because trauma mechanisms are not coded in Danish registers, and cancer patients' fractures are predominantly due to co-existing osteoporosis rather than metastases.

The control group was selected from all individuals born in 1930–1950 not meeting any of the aforementioned criteria and alive at their index date.

Data sources

Medical care costs were based on the data of the study population's utilisation of healthcare services for the period of 01.01.2000–31.12.2021 and were identified from several Danish national registers. Information on primary healthcare costs were obtained from the National Health Insurance Service Register (NHSR) [19]. The National Patient Register was used to identify all inpatient admissions, outpatient visits and diagnosis codes in accordance with the ICD-10 codes, and costs associated with delivery of these services paid for in Diagnostic Related Groups (DRGs). Data on the cost of community-filled prescription medicines was retrieved from the Danish National Prescription Register.

Consumption of municipal health and social care, *inter alia*, home help and home nursing, is registered in Statistics Denmark as hours provided per week. These hours were valued using average wages for relevant groups of healthcare professionals for care and treatment, and unskilled labour for home help. Nursing homes were valued using a monthly tariff of €4788 (2022 price level), covering care and other services provided by the municipality but not the rent which is paid by the residents themselves.

Moreover, the National Population Register, which holds detailed demographic information on all individuals residing in Denmark, was used to identify the demographic characteristics for study population, including marital status, municipality of residence, and region. Furthermore, data on emigration, death, income, educational level were also linked to the study population.

Productivity gains were estimated for the period from the beginning of observation until the individuals reach the age of 67, a conservative estimate for retirement in Denmark [20]. The estimation was done by applying the average wage of €48 per hour [21] to those who were recorded as working in each quarter during the aforementioned period. The average rate was selected to avoid introducing differences in labour market participation rate, payments, and retirement age, in order to maintain generalisability of our findings. The data on employment status was obtained from the social transfer register [22].

Statistical analyses

Propensity score matching

Propensity score matching was used to create a matched control group. The propensity score (the probability of having osteoporosis) was estimated using multiple logistic regression. The model consisted of confounders associated with an increased risk of having osteoporosis which were available in the register data. These included: age, gender, income, educational level, marital status, and Charlson comorbidity index (CCI) [23].

One-to-one nearest neighbour matching without replacement was employed [24]. Reduction of bias in the matched sample was tested with chi-squared and *t*-tests, as appropriate, as well as by comparing reduction in standardised differences [25]. All unmatched cases, both controls and osteoporosis patients, were excluded from further analyses. The index date of osteoporosis patients was the date of first diagnosis or relevant hospital admission, whichever occurred first. The index date was transferred to their matched controls such that the entire analysis population had an index date.

Estimating attributable costs

A quasi-experimental difference-in-differences (DID) approach was applied to estimate healthcare and productivity costs attributable to osteoporosis and osteoporosis fractures [26]. The total costs were compared before and after their index date. Healthcare costs included all medical (hospital care, primary care, and community-dispensed medication) and health-related social costs (home help, home nursing, rehabilitation and nursing homes). Productivity costs were defined as loss of income and only occurred until age 67 and were therefore analysed separately.

A DID analysis is a suitable choice for the analysis of observational data, where the levels of the compared groups can differ also prior to the observed event. If the treatment and control groups display parallel trends before the event, the development of the control group serves as a counterfactual to the development of the treatment group after the event, with the event being the index day. If the trend of the treatment group deviates from the counterfactual, it is assumed to be caused by the event (here occurrence of osteoporosis).

Generalised estimating equations [27, 28] with individual-level fixed effects were applied to allow for more flexibility in the common trend assumption [26]. The choice of the DID approach enables us to both control for

unobserved covariates, as each individual serves as their own control, and to circumvent the issue of right-skewed cost data which otherwise requires parametric analytical approaches or log-transformation of data and subsequent interpretation complications [29]. The assumption of parallel trends in outcomes during the pre-treatment period was tested using graphical examination and placebo tests [30]. Three DID models were fitted: unadjusted (Model 1); adjusted for sex, comorbidity, and age (Model 2); and adjusted for sex, comorbidity, age, marital status, educational level, and income (Model 3) to control for variation between the two groups unadjusted by the matching.

All costs were readjusted into 2022 Euros (€) using the net price index [21] and an exchange rate of 7.45 DKK = 1 Euro (€). All statistical analyses were performed on Stata Version 18.0 [31].

Results

Matching results

The matching process successfully matched 323,752 of 667,290 individuals from the osteoporosis group with 323,752 controls (Table 1). The matching process balanced the differences in age, sex, and income between the two groups, while statistically significant but numerically small differences in marital status, education and comorbidity remain (Table 1). After matching, both groups were made up of 73.2% women, and had a mean annual income of about €36,000. Fifty-eight percent of the osteoporosis group were married or in a partnership, compared to 56.7%

Table 1 Baseline characteristics of osteoporosis and control groups, before and after matching, people born 1930–1950

	Full sample			**Matched sample**		
Variable	Non-osteoporosis controls	Osteoporosis patients	Test	Non-osteoporosis controls	Osteoporosis patients	Test
N (%)	979,061 (75.1%)	323,763 (24.9%)		323,752 (50.0%)	323,752 (50.0%)	
Women, % (SD)	42.8 (0.495)	73.2 (0.443)	< 0.001	73.2 (0.443)	73.2 (0.442)	0.664
Mean birth year/age	1941.75	1940.24	< 0.001	1940.2	1940.2	0.002
Married (SD)	0.655 (0.433)	0.580 (0.440)	< 0.001	0.567 (0.447)	0.580 (0.440)	< 0.001
Charlson score	1.006 (1.635)	1.300 (1.713)	< 0.001	1.276 (1.785)	1.299 (1.712)	< 0.001
Education						
Lower secondary	27,369 (2.8%)	6,431 (2.0%)	< 0.001	8,572 (2.6%)	6,431 (2.0%)	< 0.001
Upper secondary	363,856 (37.2%)	141,827 (43.8%)		139,936 (43.2%)	141,825 (43.8%)	
Vocational	387,888 (39.6%)	116,380 (35.9%)		114,575 (35.4%)	116,376 (35.9%)	
Short tertiary	28,726 (2.9%)	7,413 (2.3%)		7,855 (2.4%)	7,413 (2.3%)	
Medium tertiary	122,177 (12.5%)	41,035 (12.7%)		41,520 (12.8%)	41,031 (12.7%)	
Long tertiary	49,045 (5.0%)	10,677 (3.3%)		11,294 (3.5%)	10,676 (3.3%)	
Mean annual income (SD) 2022€	40,629.892 (23,581.112)	36,077.213 (18,443.083)	< 0.001	36,008 (19,218)	36,076 (18,440)	0.147
Age at diagnosis (SD)						
All					69 (8.51)	
age by diagnosis group (n)						
Denosumab (2,651)					75 (5.50)	
Hip fracture (33,694)					72 (7.70)	
Ibandronat (401)					72 (6.13)	
Osteoporosis medication (101,189)					71 (7.44)	
Osteoporosis diagnosis (65,517)					70 (7.56)	
Upper arm fracture (33,099)					68 (7.56)	
Vertebral fracture (12,273)					69 (8.15)	
Wrist fracture (73,463)					67 (7.43)	
Zoledronate (538)					74 (5.19)	

controls. The osteoporosis group had a mean CCI score of 1.299, compared to 1.276 for the control group.

The majority of the osteoporosis group was identified through medication prescription pattern ($n = 101,189$) and a wrist fracture ($n = 73,463$). The mean age at diagnosis was 69.4 although it varied by how the diagnosis was identified, with patients identified through denosumab and zoledronic acid prescriptions being older: 75 and 74 years, respectively.

Healthcare (medical and social care) costs

Differences in unadjusted means in healthcare costs

During the observation period of 21 years, the osteoporosis group incurred higher healthcare costs in every year compared to the matched references (Fig. 1). Mean annual healthcare costs increased steadily from below €3,000 for both groups at the beginning of the observation period (age 50) until the age of 88, where the reference group's expenditure was about €20,000 per year, while the osteoporosis group expenditure reached €22,500 approximately, after age 88 the curves are crossing probably due to sample size issues. Visual inspection and placebo tests confirmed the common trend assumption (Supplementary Fig. 1).

Difference-in-difference analyses

Total annual healthcare costs attributable to osteoporosis were estimated using DID models and were found to be on average 59% higher for the osteoporosis group than for controls (OR 1.59, 95% CI 1.58–1.59) when not adjusting for any covariates, equivalent to €3,253 per year in the observation period. The difference reduced slightly to 50% higher (OR 1.50, 95% CI 1.50–1.51) but remained statistically significant when adjusting for age, gender, and comorbidity; and further to €3,097 per year higher or 1.48 times higher (95% CI 1.48–1.49) when also adjusting for income, educational level, and marital status (Table 2).

Hospital costs and social costs contributed the most the attributable costs of osteoporosis. The estimates per cost category are estimated in separate models, hence they do not add up.

The annual difference between the groups increased from below €1,000 per year at age 50, to about €12,000 per year at age 90 (Fig. 2), indicating higher osteoporosis-attributable healthcare costs with age. When assessing cost categories, the highest category was hospital costs, amounting to €2,113 per year, followed by social care costs €1,860 per year (Table 3).

We also explored the differences in costs by osteoporosis identification category. The highest costs were identified for those who were diagnosed through vertebral or hip fractures, incurring 1.62 (95% CI 1.58–1.66) and 1.85 (95% CI 1.82–1.87) times higher annual costs than controls, respectively (Table 3), when adjusting for all covariates (Model 3). Also, after adjusting for age, gender, educational level, marital status, and income, the lowest annual healthcare costs were associated with patients diagnosed through wrist fracture 1.39 times higher than for their matched controls (95% CI 1.38–1.41) (Table 3).

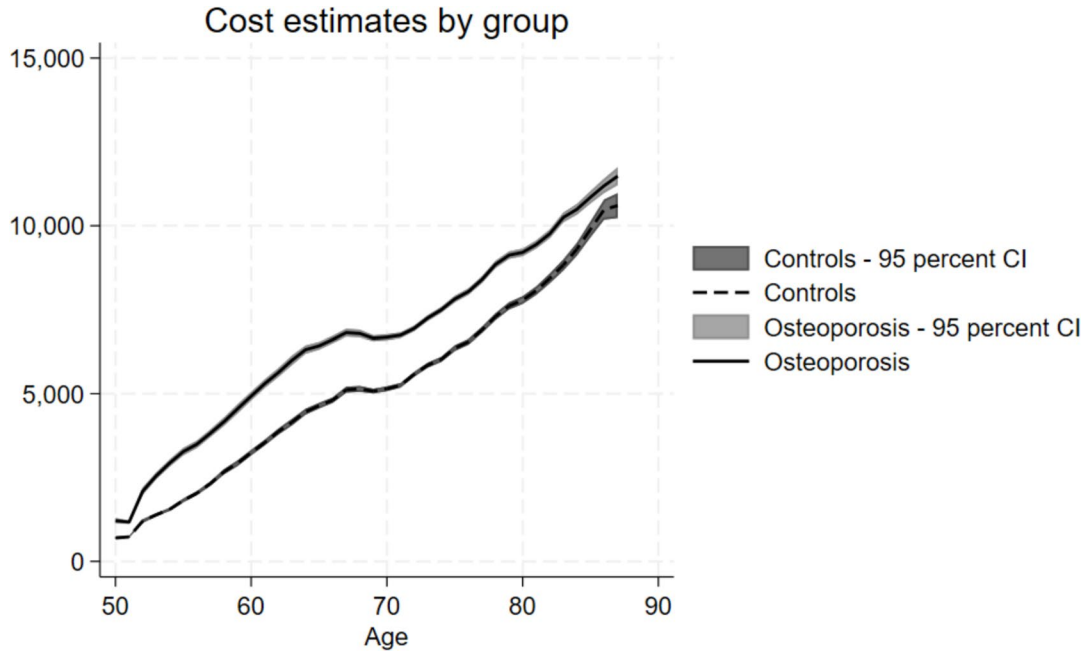

Fig. 1 Total annual healthcare (medical and social care) costs for control and osteoporosis group, 2022 EURO

Table 2 Excess annual total healthcare (medical and social care) costs (2022 Euro) attributable to osteoporosis

Total costs, 2022 EURO	Coefficients model 1	(95% conf. interval)		Coefficients model 2	(95% conf. interval)		Coefficients model 3	(95% conf. interval)	
Difference in difference	1.588	1.581	1.595	1.504	1.498	1.511	1.483	1.477	1.490
Adjusted CCI, sex, year of birth	No			Yes			Yes		
Adjusted for Income, level of education and marital status	No			No			Yes		
DiD estimate in EURO	3,252.62			3,258.83			3,097.44		
Hospital costs	1,689.98			2,193.05			2,113.05		
Primary care costs	82.08			72.22			71.51		
Pharmaceuticals costs	237.30			206.84			202.65		
Social care costs	1,243.32			1,680.57			1,860.45		

All estimates are statistically significant at < 0.0001 level

Coefficients are ORs, unless specified otherwise

The estimates per cost category do not sum to the total amount as they are estimated in separate models

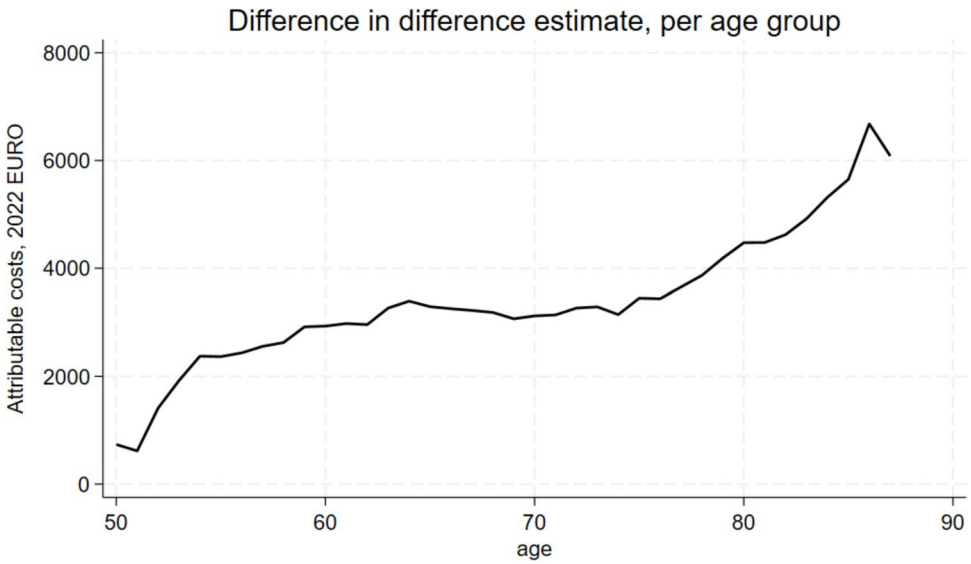

Fig. 2 Total healthcare (medical and social care) attributable to osteoporosis, 2022 EURO

Table 3 Odds ratios of excess annual total healthcare (medical and social care) costs (2022 Euro) by type of osteoporosis diagnosis

Group	Model 1	(95% conf. interval)		Model 2	(95% conf. interval)		Model 3	(95% conf. interval)	
Medication	1.560	1.549	1.572	1.450	1.439	1.461	1.434	1.424	1.445
Osteoporosis diagnosis	1.572	1.558	1.586	1.456	1.442	1.469	1.447	1.433	1.460
Upper arm fracture	1.609	1.588	1.630	1.555	1.555	1.555	1.530	1.510	1.550
Vertebral fracture	1.765	1.726	1.805	1.644	1.606	1.683	1.619	1.582	1.657
Hip fracture	1.888	1.862	1.914	1.870	1.841	1.900	1.848	1.821	1.875
Wrist fracture	1.475	1.461	1.489	1.418	1.404	1.432	1.393	1.380	1.4

All estimates are statistically significant at < 0.0001 level

Coefficients are odds ratios (ORs), unless specified otherwise

Productivity costs

Annual productivity gains were lower for the osteoporosis group compared to the matched controls from the beginning of the observation period until reaching the age of 59, after which the costs for the two groups converged and dropped significantly (Fig. 3). Then, 175,566 individuals from the control and 171,354 from the osteoporosis group were recorded as working during the productivity observation period. After age 65, most people are retired and there is no detectable difference between the groups.

The mean annual productivity gains were 18% lower for the osteoporosis group than for the reference group after controlling for age, gender, income, educational level, and marital status (OR 0.82, 95%CI 0.81–0.82) (Table 4). This corresponds to an average of €3,883 less earnings, annually, until the age of 66 for the osteoporosis group (Table 4). The gap in productivity gains between the two group narrows when approaching retirement, decreasing from around €22,500 at age 50 to around €,2000 at age 65 (Fig. 4).

Discussion

This study has identified a significant economic burden on healthcare and productivity attributable to osteoporosis in Denmark. Our estimates suggest that on average, more than €3,097 a year in healthcare costs can be attributed to having

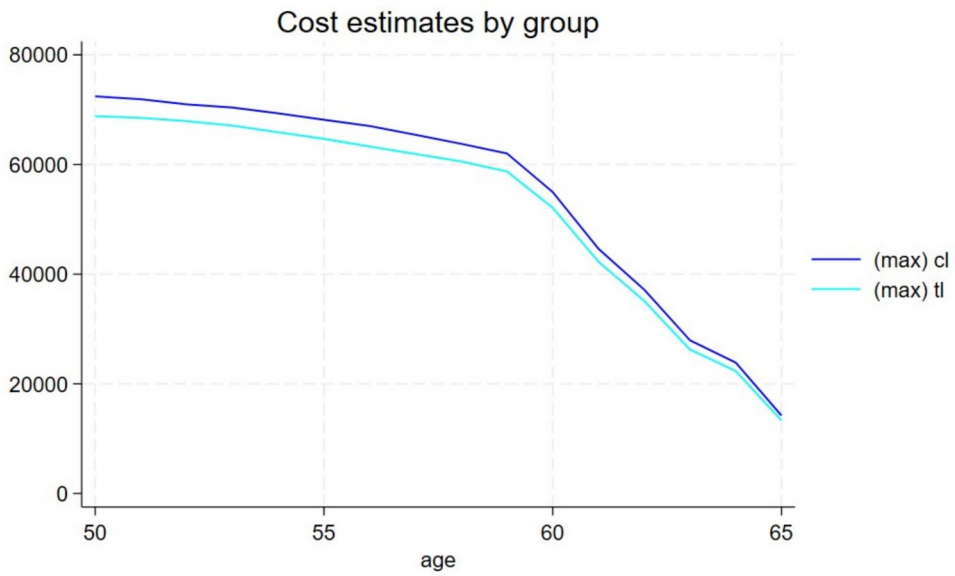

Fig. 3 Mean annual productivity costs, 2022 EURO

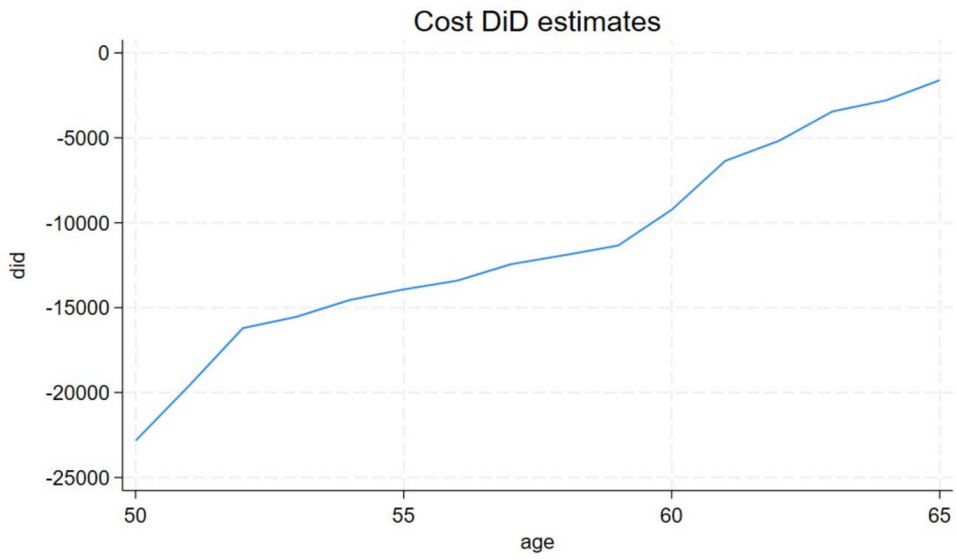

Fig. 4 Productivity losses attributable to osteoporosis, 2022 EURO

Table 4 Excess annual productivity losses (2022 Euro) attributable to osteoporosis

Productivity benefits, 2022 EURO	Coefficients model 1	(95% conf. interval)		Coefficients model 2	(95% conf. interval)		Coefficients model 3	(95% conf. interval)	
Difference in difference	0.829	0.827	0.831	0.824	0.824	0.824	0.816	0.813	0.819
Adjusted CCI, Sex, year of birth	No			Yes			Yes		
Adjusted for Income, level of education and marital status	No			No			Yes		
DiD estimate in EURO	−3974.85			−3599.73			−3883.11		

All estimates are statistically significant at < 0.0001 level

Coefficients are odds ratios (ORs), unless specified otherwise

osteoporosis or an osteoporosis-related fracture between the ages of 50 and 91. Moreover, healthcare costs attributable to osteoporosis increase by age, from less than €1,000 at age 50 to over €5,000 from 83 onwards. This presents a significant direct healthcare burden attributable to osteoporosis in Denmark.

Moreover, the economic burden of osteoporosis manifests beyond the health system and has an impact on economic productivity. We identify that osteoporosis can be attributed with a €3,883 annual loss in productivity for people between the ages of 50 and 65 (being the Danish official retirement age for most of the observed period).

These estimates are significantly higher than those previously produced for Denmark. Hansen et al. [10] report €36,000 and €26,000 lifetime osteoporosis-attributable costs in Denmark for men and women, respectively, in 2011. Cumulatively between the ages of 50 and 91, our estimates would reach €127,000 per person. However, most people decease before age 91 and it is therefore more relevant to compute the healthcare costs from age 50 to the average life expectancy, which is 83.4 years for Danish women, and 79.6 years for men in Denmark. A weighted average life expectancy would thus be 82.4 years, and the average lifetime osteoporosis-attributable healthcare costs would, consequently, arrive at just above €100,000. In addition, the average productivity costs of €3,883 per year over 16 years render €62,128 in lifetime productivity costs.

For the identified population of over 667,000 people with osteoporosis, the total annual healthcare (social and medical care) burden attributable to the disease would amount to over €2 billion. These findings are much higher than previous estimates of €850 million [7]. As our study examined real-world, individual level data, and previous estimates are based on simulation modelling, it is challenging to draw direct comparisons between the findings.

Previous research indicated that socioeconomic status had no impact on the risk of osteoporotic fractures in Denmark. [32]. Our results are likely to mirror these findings, as education had negligible impact on healthcare costs associated with osteoporosis. The cost category with the highest attributable expenditure was hospital, followed by social care, while primary care and pharmaceutical costs were relatively low. Such cost distribution is unsurprising, and supports findings from existing literature [7, 10].

We found that the highest impact on the costs associated with osteoporosis was seen in patients suffering from vertebral and hip fractures. That is not surprising as it is the clinical experience that patients with hip fractures stays longer in hospital than patients with other types of fractures and need more rehabilitation and social care after the fracture. Many hip fracture patients experience difficulties with everyday activities, and some have to move to a care home [33]. Similarly, for vertebral fractures when they come to clinical attention and are severe enough to require treatment in the hospital system, which is a requirement to be identified as a case in this analysis. These patients with severe and painful vertebral fractures often suffer those same difficulties as hip fracture patients. In addition, these two groups of patients also have a very high imminent fracture risk and therefore often experience additional fractures within a limited time period [34].

The results of our analysis further underscore the importance of preventing first and recurrent fractures in patient with osteoporosis. It has been demonstrated that Fracture Liaison Services (FLS) aiming at diagnosing and treating osteoporosis in patients presenting with fragility fractures are cost-effective [35]. Despite this, it has proven difficult getting FLS implemented at all hospitals in Denmark and so far only a few hospitals have FLSs.

Strengths and limitations

The findings of this study are subject to some limitations. The identification algorithm has been composed based on previous studies and with inputs from clinicians. As an algorithm, it may have suboptimal sensitivity and specificity. We have included fractures that are predominantly osteoporotic when occurring in this age group, although some may indeed be caused by severe accidents. We have included pharmaceuticals usually dispensed to osteoporotic patients but excluded

drugs dispensed to both cancer patients and osteoporosis patients when the administration frequency suggested that the drug was used for the treatment of cancer, for fear of misclassifying oncological patients as osteoporosis patients.

The propensity score was based on administrative observational data, and lacked some clinical predictors of osteoporosis risk, such as family history, calcium intake, and medication affecting bone metabolism, though our difference-in-differences design helps address time-invariant unobserved factors. Propensity score matching did not completely balance the differences in observed covariates between groups, in terms of education, comorbidity, and marital status. However, the absolute differences were small, and we believe that individual fixed-effects models used in the analysis sufficiently control for these differences. As this study was register-based, it was not possible to include out-of-pocket healthcare expenses associated with osteoporosis. However, as Denmark has a universal healthcare system free at the point of contact for users, with the exception of small co-payments for prescription medication which has a maximum ceiling of €610 per year [36], we believe that the costs captured in the presented analysis should capture the vast majority of healthcare costs incurred by all individuals. For the same reason, it was not possible to capture informal care costs; future studies should employ prospective data collection to capture the economic burden on informal care in osteoporosis.

It is important to acknowledge that not all included fractures were necessarily incident, as it was possible for older persons in our cohort to have experienced a fracture prior to inclusion period of 2000 to 2021. This may mean that costs of osteoporosis fractures are underestimated, making our results conservative. Moreover, the presence of the younger age groups in our cohort does represent an incident population, and propensity score matching should ensure better comparability between groups despite this limitation.

Our study only included vertebral fractures which were recorded through hospital contact. Many vertebral fractures are either asymptomatic or managed in primary care settings without hospital referral. These unreported fractures can still result in healthcare utilisation and productivity losses through chronic pain management, physiotherapy, medication use, and reduced work capacity. Therefore, our cost estimates for vertebral fractures may represent a conservative reflection of the true societal burden.

The study is also characterised by a number of strengths. The robustness and reliability of administrative register data has been documented and reported as highly suitable for health services research [11, 13, 37]. The study also utilises a unique dataset of an entire population of people with osteoporosis, observed over a 21-year period, providing a unique opportunity to draw conclusions about healthcare costs associated with the disease. Finally, we believe that the double robust methodology of matching and difference-in-difference analysis permits us to make claims of causal attribution of costs to osteoporosis.

Conclusions

Our study finds that osteoporosis and osteoporosis-related fractures are associated with higher healthcare costs and some decrements in productivity compared to their counterparts without osteoporosis. To the best of our knowledge, this is the first study to establish attributable costs in Denmark, using longitudinal individual-level data and double robust analytical approach. Our findings suggest that it is important to consider whether implementation of strategies improving prevention of osteoporosis, management, and treatment, as well as fall prevention would be efficient in the light of high costs identified.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s00198-025-07453-w.

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Data Availability Data was accessed at a secure server in Statistics Denmark and is not available publicly. Metadata is available upon request.

Declarations

Competing Interests Liza Sopina, Mette Friberg Hitz, Lau Caspar Thygesen, Benedicte Torp Ladefoged, and Marie Kruse declare that they have no conflict of interest.

Bente Langdahl declares the following: Advisory boards and lectures: Amgen, UCB, Gedeon-Richter, Entera-Bio, Samsung-Bioepis, and Angitia.

References

1. Föger-Samwald U et al (2020) Osteoporosis: pathophysiology and therapeutic options. EXCLI J 19:1017

2. Pouresmaeili F et al (2018) A comprehensive overview on osteoporosis and its risk factors. Ther Clin Risk Manag 14:2029–2049
3. Salari N et al (2021) The global prevalence of osteoporosis in the world: a comprehensive systematic review and meta-analysis. J Orthop Surg Res 16:1–20
4. Hernlund E et al (2013) Osteoporosis in the European Union: medical management, epidemiology and economic burden. A report prepared in collaboration with the International Osteoporosis Foundation (IOF) and the European Federation of Pharmaceutical Industry Associations (EFPIA). Arch Osteoporos 8(1):136
5. Clynes MA et al (2020) The epidemiology of osteoporosis. Br Med Bull 133(1):105–117
6. Svedbom A et al (2013) Osteoporosis in the European Union: a compendium of country-specific reports. Arch Osteoporos 8(1):137
7. Willers C et al (2022) Osteoporosis in Europe: a compendium of country-specific reports. Arch Osteoporos 17(1):23
8. Cortet B et al (2020) Fragility fractures in France: epidemiology, characteristics and quality of life (the EPIFRACT study). Arch Osteoporos 15:1–10
9. Alarkawi D et al (2020) Impact of osteoporotic fracture type and subsequent fracture on mortality: the Tromsø Study. Osteoporos Int 31:119–130
10. Hansen L et al (2013) A health economic analysis of osteoporotic fractures: who carries the burden? Arch Osteoporos 8:126
11. Kruse M, Christiansen T (2011) Register-based studies of healthcare costs. Scand J Pub Health 39(7_suppl):206–209
12. Erlangsen A, Fedyszyn I (2015) Danish nationwide registers for public health and health-related research. Scand J Public Health 43(4):333–339
13. Lynge E, Sandegaard JL, Rebolj M (2011) The Danish national patient register. Scand J Public Health 39(7_suppl):30–33
14. Wallach Kildemoes H, Toft Sørensen H, Hallas J (2011) The Danish national prescription registry. Scand J Public Health 39(7_suppl):38–41
15. Lippuner K, Golder M, Greiner R (2005) Epidemiology and direct medical costs of osteoporotic fractures in men and women in Switzerland. Osteoporos Int: J Established as Result of Cooperation Between the European Foundation for Osteoporos Nat Osteoporos Found USA 16(Suppl 2):S8–S17 https://doi.org/10.1007/s00198-004-1696-0
16. Roerholt C, Eiken P, Abrahamsen B (2009) Initiation of anti-osteoporotic therapy in patients with recent fractures: a nationwide analysis of prescription rates and persistence. Osteoporos Int 20(2):299–307
17. Sundhedsdatastyrelsen (2018) Prævalens, incidens og behandling i sundhedsvæsenet for borgere med osteoporose. https://sundhedsdatastyrelsen.dk/media/16320/Bilagspublikation_osteoporose.pdf
18. LeBoff MS et al (2022) The clinician's guide to prevention and treatment of osteoporosis. Osteoporos Int 33(10):2049–2102. https://doi.org/10.1007/s00198-021-05900-y
19. Sahl Andersen J, De Fine Olivarius N, Krasnik A (2011) The Danish National Health Service Register. Scand J Public Health39(7_suppl):34–37
20. OECD (2023) Pensions at a Glance 2023. https://www.oecd.org/en/publications/2023/12/pensions-at-a-glance-2023_4757bf20.html
21. Statistics Denmark (2023) StatBank. Available from: https://www.statistikbanken.dk/statbank5a/SelectTable/Omrade0.asp?PLanguage=1. Accessed Jan 2024
22. Hjollund NH, Larsen FB, Andersen JH (2007) Register-based follow-up of social benefits and other transfer payments: accuracy and degree of completeness in a Danish interdepartmental administrative database compared with a population-based survey. Scand J Public Health 35(5):497–502
23. Charlson ME et al (1987) A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 40(5):373–383
24. Caliendo M, Kopeinig S (2008) Some practical guidance for the implementation of propensity score matching. J Econ Surv 22(1):31–72
25. Austin PC (2009) Balance diagnostics for comparing the distribution of baseline covariates between treatment groups in propensity-score matched samples. Stat Med 28(25):3083–3107
26. Wing C, Simon K, Bello-Gomez RA (2018) Designing difference in difference studies: best practices for public health policy research. Annu Rev Public Health 39:453–469
27. Cui J, Qian G (2007) Selection of working correlation structure and best model in GEE analyses of longitudinal data. Commun Stat Simul Comput 36(5):987–996
28. Hanley JA et al (2003) Statistical analysis of correlated data using generalized estimating equations: an orientation. Am J Epidemiol 157(4):364–375
29. Jones AM et al (2013) Applied health economics, vol 19, 2nd edn. Routledge. https://doi.org/10.4324/9780203102411
30. Lechner M (2011) The estimation of causal effects by difference-in-difference methods. Found Trends® in Econom 4(3)165–224
31. StataCorp (2023) Stata statistical software: release 18. https://doi.org/10.1561/0800000014
32. Holmberg T et al (2019) Socioeconomic status and risk of osteoporotic fractures and the use of DXA scans: data from the Danish population-based ROSE study. Osteoporos Int 30:343–353
33. Hallberg S et al (2024) Association between institutionalization by 4 months post-discharge walking capacity and lean body mass in elderly hip fracture patients: evidence from a Swedish Registry Based Study. SAGE Open Medicine 12:20503121241258410
34. Johansson H et al (2017) Imminent risk of fracture after fracture. Osteoporos Int 28:775–780
35. Mclellan AR et al (2011) Fracture liaison services for the evaluation and management of patients with osteoporotic fracture: a cost-effectiveness evaluation based on data collected over 8 years of service provision. Osteoporos Int 22:2083–2098
36. Danish Medicines Agency (2023) Reimbursement thresholds. Available from: https://laegemiddelstyrelsen.dk/en/reimbursement/calculate-reimbursement/reimbursement-thresholds/. Accessed Jul 2024
37. Thygesen LC, Ersbøll AK (2011) Danish population-based registers for public health and health-related welfare research: introduction to the supplement. Scand J Public Health 39(7_suppl):8–10