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Socioeconomic inequality in drug reimbursement during end-of-life care:

A nationwide study

Research Year Report

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Preface

This report is based on a study conducted during my research year at the Department of Clinical Epidemiology, Aarhus University Hospital, from February 2017 to February 2018.

A special thanks to my main supervisor Søren Paaske Johnsen for patiently guiding me through the world of epidemiology and for giving me the opportunities to make the most of my research year. Thank you, Mette Asbjoern Neergaard and Mette Kjærgaard Nielsen, for contributing with your clinical knowledge and for continuously being available with constructive feedback. Thank you, Anne Høy Seemann Vestergaard for discussing my thoughts and answering all my questions. Also, I must express my thanks to Anders H. Riis for his statistical expertise and endless patience, and to Pia K. Kristensen for support and company during my first conference presentation.

During my research year, I had the pleasure of a one-month stay at the Dartmouth Institute for Health Policy and Clinical Practice. I appreciate the hospitality and supervision by professor David Goodman and the help Julie Doherty provided by organizing my stay.

Finally, a massive thank you to my fellow research year students for contributing with laughter and joy to my everyday life. I'm deeply grateful for sharing this year with you; a year full of biostatical frustrations and wine-full celebrations.

Cecilie Daugaard, February 2018

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List of abbreviations

CCI	Charlson Comorbidity Index
CI	Confidence interval
CRS	Civil Registration System
DRTI	Drug reimbursement due to terminal illness
EOL	End-of-life
GP	General practitioner
ISCED	International Standard Classification of Education
PR	Prevalence ratio

List of contents

Abstract

Background: In Denmark, terminally ill patients have the right to complete drug reimbursement due to terminal illness (DRTI), which may be a proxy marker of planned end-of-life care. The aim was to examine socioeconomic differences in DRTI status among Danish terminally ill patients.

Methods: Using Danish nationwide registries, we identified all patients dying from cancer, dementia, ischemic heart disease, chronic obstructive pulmonary disease, chronic liver disease, congestive heart failure, diabetes or stroke in 2006-2015. We computed prevalence ratios (PRs) of DRTI adjusted for age, gender, comorbidity, cause of death and residency in patients with different socioeconomic factors (i.e. education, income, cohabiting status, migrant status, employment).

Results: Overall, 27.9% of the patients received DRTI. A substantial difference in likelihood of receiving DRTI was observed when comparing patients with the most advantageous versus the worst off socioeconomic profile (adjusted PR 1.36; 95% CI: 1.10-1.67). The probability of DRTI was higher among patients with high compared with low income (adjusted PR:1.22, 95% CI 1.17-1.26). Also, living with a partner and being immigrant or descendant of such were characteristics associated with higher probability of DRTI compared with living alone and of Danish origin, whereas employment was associated with lower probability of DRTI compared with unemployment.

Conclusion: Socioeconomic position is associated with the likelihood of receiving DRTI, which indicates that planned end-of-life care is not equally accessible.

Dansk resumé

Baggrund: Alle danske patienter har ret til terminaltilskud. Tilskuddet kan muligvis anvendes som en markør for planlagt palliativt forløb.

Metode: Ved brug af danske landsdækkende registre identificerede vi patienter døde af kræft, demens, iskæmisk hjertesygdom, kronisk obstruktiv lungesygdom, kronisk leversygdom, hjertesvigt, diabetes og apopleksi i årene 2006-2015. Vi udregnede prævalens ratioer (PR) for terminaltilskud justeret for alder, køn, komorbiditet, dødsårsag og bopæl blandt patienter med forskellige socioøkonomisk baggrund (uddannelse, indkomst, samlevende status, migrant status og arbejdsmarkedstilknytning).

Resultater: I alt modtog 27,9% af de 307.188 afdøde patienter terminaltilskud. Patienter med den mest fordelagtige socioøkonomiske profil havde større sandsynlighed for at modtage terminaltilskud ift. patienter med den mindst fordelagtige socioøkonomiske profil (justeret prævalensratio: 1.36, 95% CI: 1.10-1.67). Sandsynligheden for at modtage terminaltilskud var lavere for patienter i arbejde sammenlignet med arbejdsløse patienter, hvorimod høj indkomst, at bo med en partner og at være indvandrer eller efterkommer heraf var faktorer associeret med højere sandsynlighed for terminaltilskud ift. lav indkomst, at bo alene og være af dansk oprindelse.

Konklusion: Der er socioøkonomisk variation i tildeling af terminaltilskud, hvilket indikerer at planlagt palliativt forløb ikke tilfalder alle patienter.

Manuscript

Introduction

Socioeconomic inequality poses a serious challenge to public healthcare systems in general and has also been reported within end-of-life care, e.g. in relation to place of death and access to specialised end-of-life care[1–5]. A structured planning process of the end-of-life period may potentially facilitate high-quality end-of-life care for all patients. For instance, most terminally ill patients prefer care at the end of life and death to take place at home, [6–12] and this should, consequently, be planned and facilitated whenever possible. However, planned end-of-life care requires recognition of the approaching death, which is challenged by variation in illness trajectories, prognosis and treatment options. [13,14]

When a physician in Denmark asses the patient's life expectancy to be short and no further curative treatment can be offered, the physician may apply for drug reimbursement due to terminal illness (DRTI). [15] DRTI aims to ensure adequate medication for non-hospitalised patients in line with the free-of-charge medication provided for hospitalised patients, as patients with DRTI receive all prescription medicine free of charge. [16] Thus, DRTI may be a proxy marker of initiated, planned end-of-life care.

To our knowledge, no previous study has investigated whether there are socioeconomic inequalities in DRTI allocation. Therefore, the aim of this study was to examine the association between socioeconomic position and registration with DRTI among terminally ill patients in Denmark. We hypothesised that higher socioeconomic position, as reflected by higher level of education, higher income, being cohabitating, of Danish origin, and employed, would be associated with a higher chance of receiving DRTI.

Methods

Study design and setting

A register-based cross-sectional study was conducted among all adult decedents in Denmark who died of cancer, dementia, ischemic heart disease, chronic obstructive pulmonary disease, chronic liver disease, congestive heart failure, diabetes or stroke in 2006 through 2015.

The register data was linked by a unique 10-digit personal identification number, which all citizens receive upon birth or immigration. [17–19] The Danish healthcare system is tax-based and has universal coverage of all 5.7 million residents, thus providing free hospital and hospice services. When patients are treated outside hospital, medicine expenses are only partly subsidised. [16] However, all patients have the right to receive complete DRTI when life expectancy is short (few weeks to months) and no curative treatment can be offered. [15]

The study was approved by the Danish Data Protection Agency (Central Denmark Region: record no. 1-16-02-407-14) and all data was linked and stored at Statistics Denmark. According to Danish law, registry-based studies do not require ethical approval.

Decedents

Using the Danish Registry of Causes of Death, all decedents aged 18 years and above registered with cancer, dementia, ischemic heart disease, chronic obstructive pulmonary disease, chronic liver disease, congestive heart failure, diabetes or stroke as the underlying cause of death in the 2006-2015 period were identified. The registry contains data based upon death certificates coded by physicians, including information on the date and place of death and immediate, contributing and underlying causes of death. [20]

Socioeconomic position

Socioeconomic position was defined by five factors: education, income, cohabiting status, migrant status and employment. Data on education and income was obtained from the education and income registries by Statistics Denmark. [21,22] Based on the International Standard Classification of Education (ISCED 2011), [23] education was categorised into three levels according to highest completed education: low (none or less than elementary school, ISCED level 0-2), middle (more than elementary school but less than bachelor level or equivalent, ISCED level 3-4) and high (equivalent to bachelor level or more, ISCED level 5-8). Income was defined by mean annual family income during a five-year period before death and categorised into tertiles of increasing income. Information on cohabiting status (living alone/living with a partner) and migrant status (non-immigrant/immigrant or descendant of such) was obtained from the Civil Registration System (CRS). [17,24] Information on employment one year prior to death was achieved from the Integrated Database for Labour Market Research, established by the Statistics Denmark in 1980. [25]

Individual drug reimbursement and palliative drug consumption

Information on drug reimbursement including DRTI status and redemption of prescription medicine was obtained from the Register of Medicinal Product Statistics. [26] This registry was established in 1994 by the Danish Medicines Agency and holds information on all pharmacy sale of medicinal products and information on drug reimbursement status at time of redemption.

To explore if the prescribed pattern of palliative medicine differed according to DRTI status, we achieved out-of-hospital data on redeemed drugs often used in palliative trajectories: opioids, anxiolytics, sedatives and antidepressants (anatomical therapeutic chemical codes: N02A, N05B, N05C and N06A) during the last month prior to death. This time period was chosen to capture medicine

related to palliative care, since the median survival time after DRTI registration is two months. [27]

Data included number of prescriptions as well as type and cost of drugs.

Patient characteristics

Patient characteristics included cause of death (diagnosis), information on age, gender, residency (municipality/region) and comorbidity level. Information on cause of death was obtained from the Danish Registry of Causes of Death, whereas information on age, gender and residency was obtained from the CRS. Comorbidity level was assessed using the Charlson Comorbidity Index (CCI) that comprises 19 selected and weighted conditions according to their potential influence on mortality. The CCI data was obtained from the National Registry of Patients and computed using all diagnoses in relation to hospitalisation and outpatient visits in a period of five years prior to death. [28,29] The weights of the 19 conditions were summed to a score, excluding cause of death. The CCI was included as a continuous variable in the adjusted analysis and presented as three comorbidity levels: a score of 0 (no previous record of diseases included in the CCI); a score of 1–2; and a score of 3 or more.

Statistical analyses

The association between the socioeconomic factors and DRTI prevalence was calculated as crude and adjusted prevalence proportion ratios (PRs) and 95% confidence intervals (95 % CIs) using generalised linear models with log link function and Poisson distribution.[30] In the adjusted analysis, we included information on age, gender, cause of death (diagnosis) and comorbidity. We clustered individuals within municipalities to account for geographical variation in treatment practice. Because of concerns about possible collinearity among the socioeconomic factors, we constructed

five separate adjusted models, each incorporating only one socioeconomic factor and a final mutually adjusted model including all five socioeconomic factors. In addition, we created a composite measure of socioeconomic profile by combining all five socioeconomic factors into two socioeconomic status groups: A socioeconomic profile associated with the lowest probability of DRTI ("worst off socioeconomic profile") and a socioeconomic profile associated with the highest probability of DRTI ("best off socioeconomic profile").

The potential interaction of the socioeconomic factors was investigated by repeating the analyses while stratifying for each level of education and employment. In addition, the analyses were repeated by stratifying patients by cause of death into cancer and non-cancer patients. Moreover, we made a sensitivity analysis restricted to cancer patients who were not admitted to hospital within the last month prior to death.

The number, type and costs of redeemed palliative prescription drugs were compared within the last month prior to death according to DRTI status for the entire study population. A sensitivity analysis of redeemed palliative drugs was also made only including cancer patients who were not admitted to hospital within the last month prior to death.

We addressed missing data by the missing indicator method. In particular, data on education was incomplete, as it was not systematically registered before 1973. The analyses were repeated using the multiple imputation method to impute the missing data on education (using all available data presented in Table 1 including outcome data). [31]

Data were analysed using Stata 14.2 (StataCorp LP, College Station, TX, USA)

Results

We identified 314,281 patients above 18 years of age who died from the eight selected diseases between 2006 and 2015. As shown in Figure 1, patients with incomplete CRS data, incomplete information on purchased medication or unknown DRTI status from the Register of Medicinal Product Statistics were excluded (n=7,093 patients), leaving 307,188 patients for further analysis.

Of the included decedents, 27.9% had been allocated to DRTI prior to death, and 94.0% of these died from cancer (Table 1). Apart from information on education and income, data were almost entirely complete for all variables.

DRTI and socioeconomic factors

The proportion of patients with DRTI was 29.3% for patients with a "worst off socioeconomic profile" and 62.9% for patients with a "best off socioeconomic profile". This corresponded to an adjusted PR for DRTI of 1.36 (95% CI 1.10-1.67) among patients with a "best off socioeconomic profile" when compared with patients with a "worst off socioeconomic profile" (Table 2).

The adjusted analysis showed no association between education and DRTI. In contrast, higher income was associated with DRTI status, i.e. the adjusted PR for DRTI was 1.16 (95% CI 1.14-1.20) for patients with middle income and 1.22 (95% CI 1.17-1.26) for patients with high income compared with patients with low income. The adjusted PR for DRTI was 1.18 (95% CI 1.15-1.22) among patients living with a partner compared with living alone. For immigrants or descendants of such the adjusted PR was 1.04 (95% CI 1.01-1.07) compared with non-immigrants. Employment status was also associated with DRTI status in the adjusted analyses, since the PR for DRTI among

patients who were employed was 0.86 (95% CI 0.84-0.87) compared with patients who were unemployed.

The results were not materially different in the sensitivity analyses using multiple imputation for handling patients with missing data (data not shown). The association between education, income, cohabiting status and employment and DRTI was stronger among decedents of non-cancer diseases compared with decedents of cancer (Table 3). The sensitivity analysis restricted to cancer patients who were not hospitalised one month prior to death confirmed the findings in the main analysis (data not shown).

Table 4 presents results from the analyses stratified by employment and education. Among unemployed patients, the adjusted PR for DRTI was 1.36 (95% CI 1.29-1.44) for patients with high compared with low income. Among patients who had an academic or leadership job position the adjusted PR for DRTI was 1.08 (95% CI 0.98-1.20) for patients with high compared with low income. When we stratified for education, we found a similar pattern, i.e. income was less associated with DRTI among the high-educated patients.

DRTI and redeemed prescriptions during end-of-life care

The proportion of patients who redeemed ten or more palliative medications at general pharmacies within the last month prior to death was 15.0% among patients with DRTI and 2.6% among patients without DRTI (Table 5). Among patients with DRTI, 34.4% redeemed five or more opioids, whereas this proportion was 5.8% among patients without DRTI. The differences in redeemed prescriptions persisted when we restricted the analysis to cancer patients who were not admitted to hospital within the last month prior to death (results not shown).

Discussion

Main findings

In this large nationwide study, we found DRTI allocation to vary across socioeconomic position. High income, living with a partner, being immigrant or descendants of such, and being unemployed, were all factors associated with a substantially increased probability of receiving DRTI.

Strengths and weaknesses

A major strength of this study is the population-based design with prospective data collection, causing a low risk of selection and information bias. [32] In a period of ten years, we included all patients dying from eight illnesses accounting for two thirds of all deaths in Denmark. We were able to link all data, including comprehensive socioeconomic data, on individual level and adjust for age, gender, cause of death, comorbidity and residency. However, a risk of unmeasured confounding remains.

We only obtained information on prescriptions redeemed at general pharmacies, whereas medication administered during hospitalisation was not available. In addition, we were unable to ascertain in-hospital or in-hospice end-of-life care, differences in illness trajectories and acuteness of death. The lack of such information might have been a limitation. However, by sensitivity analysis restricted to non-hospitalised cancer patients, we aimed to eliminate potential confounding.

What this study adds?

To our knowledge, no previous study has investigated socioeconomic inequalities in DRTI allocation, and data on socioeconomic inequalities in access to early planned out-of-hospital end-of-life-care are sparse.

In accordance with our findings, previous studies have shown high income, being married, immigrant/descendants of such and unemployed/being student/receiving social security to be associated with increased probability of dying at home and access to outreach specialised palliative care teams. [2–5] However, these studies only included cancer patients and did not provide information on nationwide populations. Hence, our study provides new knowledge on patterns of inequality that may apply to planned end-of-life care in general.

All residents have free access to services in the Danish tax-financed healthcare system, and DRTI serves as a financial aid. Therefore, it seems contradictory that patients with a high income were more likely to receive DRTI than patients with a low income. However, among patients with academic or leadership job position or high educational level, the association between income and DRTI was less prominent. This suggests that patients with other socioeconomic resources reflected by job position or education are more likely to receive DRTI independent of income level. Nevertheless, palliative care needs may tend to be unrecognized in patients with low income.

To apply for DRTI, an involved physician must recognise transition into terminal phase. However, physicians often overestimate the remaining lifetime, [33] which may hinder end-of-life planning and delay DRTI application. The finding of lower likelihood of receiving DRTI among employed compared with unemployed may support the hypothesis that physicians find it difficult to estimate remaining lifetime for patients with a fast decline in physical function exemplified by sudden labour market exit. Hence, as patients may differ in clinical condition and predictability of death, they may not be equally eligible for planned end-of-life care and DRTI.

Among patients allocated to DRTI, most died from cancer (94%). When stratifying by cause of death, we found the association between socioeconomic factors and DRTI to be more prominent among non-cancer patients. Also, among non-cancer patients we found an association between education and DRTI that was not present among cancer patients. A reason for these findings may be,

that health professionals tend to focus on cancer patients while overlooking palliative needs in non-cancer patients. [34,35] Whereas cancer patients in general are more likely to receive DRTI, it seems that among non-cancer patients it is even more likely for highly-educated patients to receive DRTI. Thus, palliative care needs in lower educated non-cancer patients might be unsupported.

The finding of difference in redeemed palliative medication according to DRTI status supports our interpretation of DRTI as a marker of planned end-of-life care. However, as the difference was mainly due to opioid prescriptions, it might reflect that patients without DRTI were treated with opioids during hospital admissions. Nevertheless, when we restricted the analysis to non-hospital-ised cancer patients, the differences remained, indicating an actual variation in medication between patients with and without DRTI. Thus, even though the DRTI allocation is a financial aid for medicine expenses, it may have wider implications as a marker of planned end-of-life care.

Our findings suggest unequal access to planned end-of-life care. However, enhanced focus may decrease inequality between patients with high and low socioeconomic position. Therefore, this study may increase awareness of inequality and thereby help health professionals focus on vulnerable terminally ill patients.

We have proposed DRTI to be a marker of planned end-of-life care. Additional research is needed on differences in end-of-life care between patients with and without DRTI including hospital admission rates, access to specialised palliative care and place of death. In addition, efforts are warranted to further understand the mechanisms of inequality in a free-access healthcare system by exploring geographical variation in planned end-of-life care.

Conclusion

We found socioeconomic position, i.e. high income, living with a partner, being immigrant or descendant of such and unemployment to be associated with increased probability of DRTI allocation,

despite a tax-financed free-access healthcare system. DRTI may be a proxy marker of planned end-of-life care. Hence, our results suggest, that planned end-of-life care is not equally accessible for all terminally ill patients. Efforts are warranted to further explore mechanisms of inequality to ensure appropriate end-of-life care.

Supplementary

Extended background

Variation in end-of-life care

Optimal and effective healthcare at the end of life is of great importance among terminally ill patients. Since the Danish healthcare system is tax-based and has universal coverage of all citizens, end-of-life care is in principle equally accessible for all patients. [36,37] However, examples of socio-economic inequalities in the Danish healthcare system has been reported in recent years, including inequalities regarding place of death and the use of specialised palliative care for end-of-life patients. [1–5]

Drug reimbursement

All expenses during hospital and hospice admission are covered by the Danish healthcare system. Also, the Danish health care system provides drug reimbursements, which are structured into two groups: general partial drug reimbursements which activate when annual drug expenses reaches above 130 euro and patient specific drug reimbursements. Terminally ill patients have their medicine expenses covered by a patient specific drug reimbursement due to terminal illness (DRTI). [15] The DRTI can be applied for by a physician, if the patient has no curative treatment options and has a short life expectancy (few weeks to months), and it is approved by the Danish Medicines Agency within 1-2 workdays. It entitles patients to receive all prescription medicine free of charge at general pharmacies and thus ensures medical care for patients treated at home in line with the care provided for hospitalised patients. To receive DRTI, however, it is a prerequisite that an involved physician recognises and verbalises the approaching of terminal phase, which is challenged by variation in illness trajectories, prognosis and treatment options. [13,14]

13

During the last decade, DRTI has annually been allocated to approximately 10,000-15,000 patients, corresponding to 20-30% of all Danish decedents. [38] DRTI may be essential to ensure high quality end-of-life care outside hospital. However, to our knowledge, no study has investigated inequalities in the use of DRTI, including whether it benefits all terminally ill patients equally irrespective of socioeconomic background.

Methodological considerations

Study design

We designed a cross-sectional study including patients deceased from cancer, dementia, ischemic heart disease, chronic obstructive lung disease, chronic liver disease, congestive heart failure, diabetes or stroke in the period 2006-2015. These eight illnesses are responsible for more than two thirds of all deaths in the Danish population. [39]

Cross-sectional studies are used to assess the presence of the outcome of interest, why they are also known as prevalence studies. All study information refers to a given time-period, in this study a 10-years period. The cross-sectional design is not able to determine causation, as it cannot establish the direction of effect. Nevertheless, it can be used to identify associations and may serve as a basis for further examination of causal pathways. [40] In this present study, some of the obtained exposure information pertains more than one point in time. For instance, the socioeconomic factor "income" is defined as the mean yearly family income in a five-year period prior to death. Thus, the causal action of the exposure (income) appears prior to the subsequent outcome (allocation of DRTI), why causation is determined. To summarize, the cross-sectional design was an appropriate, valid and affordable method for this study. The feasibility was mainly due to the Danish registries with high completeness, containing data from the universal tax-financed healthcare system, which aims to provide all Danish residents with free and equal healthcare. [36,37]

The aim of this study was to examine the association between socioeconomic position and DRTI allocation among terminally ill patients in Denmark. We hypothesised that higher socioeconomic position, as reflected by higher level of education, higher income, being cohabitating, of Danish origin, and employed, would be associated with a higher chance of receiving DRTI.

DRTI as a marker of planned end-of-life care

In the present study, we used the Danish DRTI as a marker of planned end-of-life care. To illustrate the concepts of the Danish healthcare system, our study assumptions, and expectations, we created a conceptual framework (Supplemental Figure 1). The framework specifies the mechanism of DRTI allocation at both patient and physician level, municipality and regional level. However, for this study, we only included the variables specified in green boxes at patient and physician level i.e. place of residency, patient characteristics, diagnosis and comorbidity, socioeconomic position and DRTI.

As illustrated in the framework, three circumstances may precede DRTI application: illness specific care, illness perception and preferences for end-of-life care. Firstly, as a physician must apply for DRTI, the extend of hospital- and physician engagement and contact ("illness specific care") may affect the probability of receiving DRTI. Secondly, the physician and the patient must acknowledge the approaching terminal phase ("illness perception"), before the physician can proceed to DRTI application. Finally, the patient's preferences for end-of-life care ("preferences for EOL care"), including where end-of-life care should take place, may affect the application of DRTI. Hence, several circumstances, which may indicate high-quality planned end-of-life care, precede DRTI application. To validate DRTI as a marker of planned end-of-life care, we compared the number, type and costs of redeemed palliative prescription drugs within the last month prior to death according to DRTI status for the entire study population. Our hypothesis was, that if quality of end-of-

15

life care differed according to DRTI status, this would also be reflected in differences in medication during end-of-life.
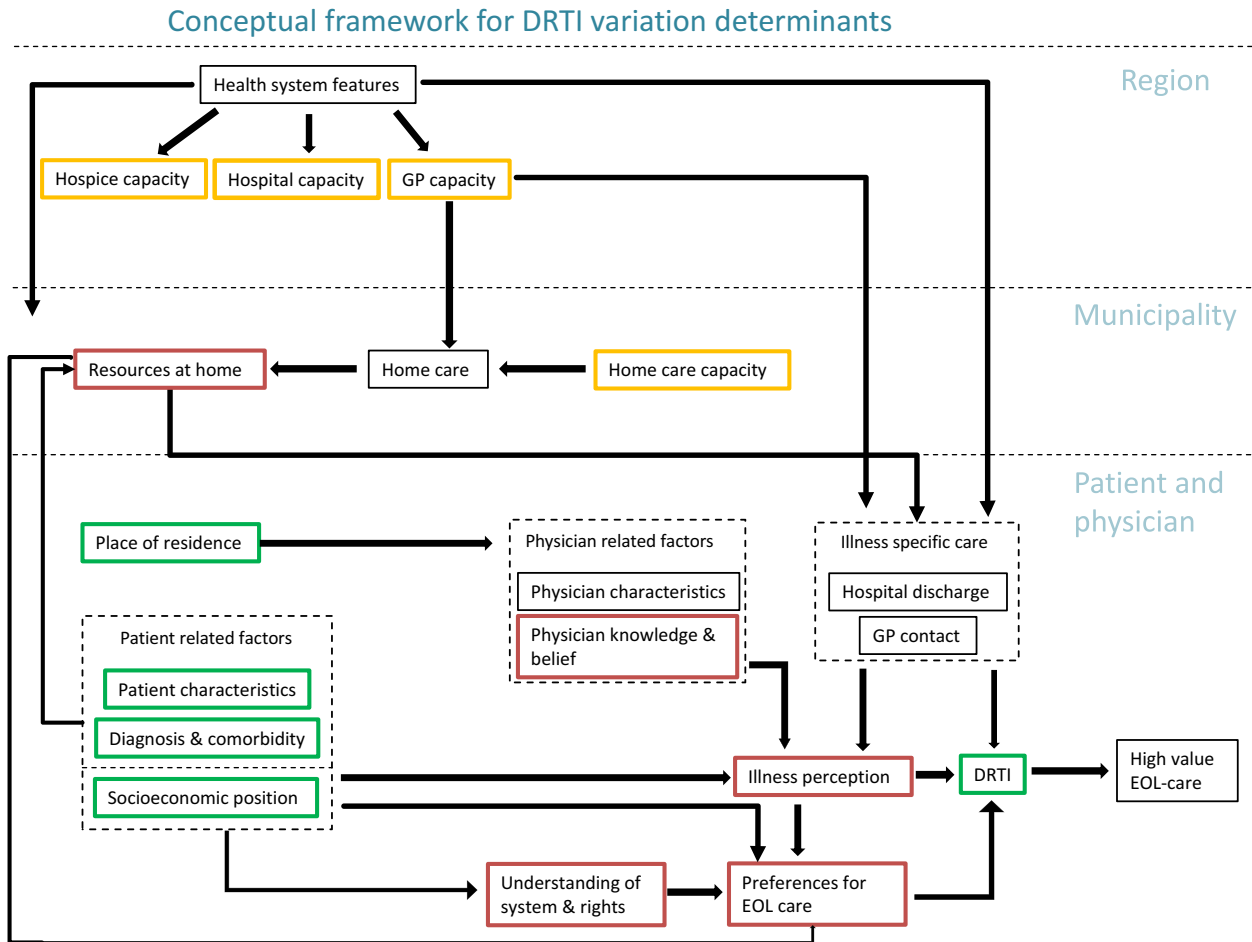
Supplemental Figure 1
Conceptual framework for DRTI variation determinants. Green boxes contain variables included in the model, yellow boxes contain variables that are not included and red boxes contain unmeasurable variables.
GP: general practitioner. EOL: end-of-life.

Statistical analysis

Initially, we made descriptive statistics by tabulating cause of death, socioeconomic factors and co-variates by DRTI status. The association between the socioeconomic factors and the prevalence of DRTI was calculated as crude and adjusted prevalence proportion ratios (PRs) using generalized linear models with log link function and Poisson distribution. [30] The Poisson distribution is a probability distribution that applies to count data. [41] In the present study, the events (DRTI) are counted across a number of patients. Also, several sensitivity analyses were made i.e. applying different methods to handle missing data, stratifying for education, income, employment and death cause and restricting the study participants or study time-period. The data was analysed using Stata 14.2 (StataCorp LP, College Station, TX, USA).

Missing values

Data was obtained from nationwide health registries. As the registries have a high completeness, we only experienced missing data on few variables. Information on medicine purchase and reimbursement status was lacking for 1.5% of the study population. Information on mean family income and education level was lacking for 14.5% and 1.4% of the study population, respectively.

Missing values can be categorised into three groups according to the probability of being missing: missing completely at random, missing at random, and missing not at random. [42] For instance, 84% of patients with missing information on education were living alone. Hence, the probability of missing data depends on already observed information, why the missing data may be characterised as missing at random. [31] We handled the missing data by the missing indicator method, where missing data is grouped into a "missing" category. However, this method may be subject to bias. [31] Consequently, we repeated the analyses using the multiple imputation method to impute the missing data on education (using all available data presented in Table 1 including outcome data), which gener-

ated 20 imputed datasets. We also used the complete case method excluding all patients with missing information on any variable. Both sensitivity analyses generated results similar to the main analysis, in this case suggesting the strength of the missing indicator method.

Correlation

We defined socioeconomic status by five factors: highest achieved education, mean yearly family income in a five-year period prior to death, cohabiting status and migrant status at time of death, and employment status one year prior to death. These factors may, however, be dependent and hence strongly correlated. For instance, high educational level may lead to a high job position, which may lead to high income. Inclusion of highly correlated exposure variables in a regression model can give the impression, that neither one is associated with the outcome, even when each are individually associated with the outcome. [43] Because of concerns that the socioeconomic factors were collinear, we ran different models predicting the prevalence ratios of DRTI. Initially, we ran five separate adjusted models each incorporating only one socioeconomic factor. Finally, we ran a mutually adjusted model incorporating all socioeconomic factors. We found no substantial change in the PR estimates among the different models, which suggests that the socioeconomic factors are not significantly collinear. Hence, they were all included in the final regression model.

Additional strengths and limitations

Selection bias

Selection bias is a systematic error that can be introduced through selection of subjects at the level of study entry or through loss to follow up. [40] We used the Danish Registry of Causes of Death to provide information on cause of death. The coding of death by physicians is prone to erroneous registration, however, selection bias could only occur, if decedents included in the study had a different

association between socioeconomic status and allocation of DRTI than non-included decedents, which is most unlikely. [20]

Information bias

Information bias is a systematic error. It can arise if the collected data is erroneous and thus information is misclassified. Misclassification is categorised as non-differential if it is unrelated to other study variables and it can force estimates towards no association. A misclassification is differential if it is related to other study variables and it can cause a false association. [40]

Information on DRTI (outcome) was obtained from the Register of Medicinal Product Statistics, which holds complete information on all sales of prescription medication at general pharmacies. At every sale, drug reimbursement status is recorded. However, we were only able to ascertain DRTI status among patients with a medicine purchase within the year prior to death. Consequently, a differential misclassification could occur, if the likelihood of medicine redemption differed according to socioeconomic position (exposure), e.g., if patients with high socioeconomic position more often redeemed any medicine during their last year. However, as only 1.3% of the decedents (n=3,927) lacked data on prescription medication redemption one year prior to death, we found it unlikely to cause any bias. Overall, data on exposure and covariates was collected independent from the study and in a prospective manner, without any knowledge about various outcomes. Hence, differential misclassification is most unlikely.

Confounding

Confounding can be defined as a confusion of effects. It occurs if the effect of the exposure is mixed with the effect of another variable. Thus, a confounder variable must be associated with the exposure and the outcome without being an effect of the exposure. [40]

By using multivariate analysis, we could include relevant pre-specified confounders i.e. age, gender, comorbidity, death cause and residency, as these factors are known from previous studies to influence end-of-life care. [34,35,44–47] To asses biasing pathways, we created a Directed Acyclic Graph (DAG), which confirmed our inclusion of pre-specified confounders (Supplemental Figure 2).
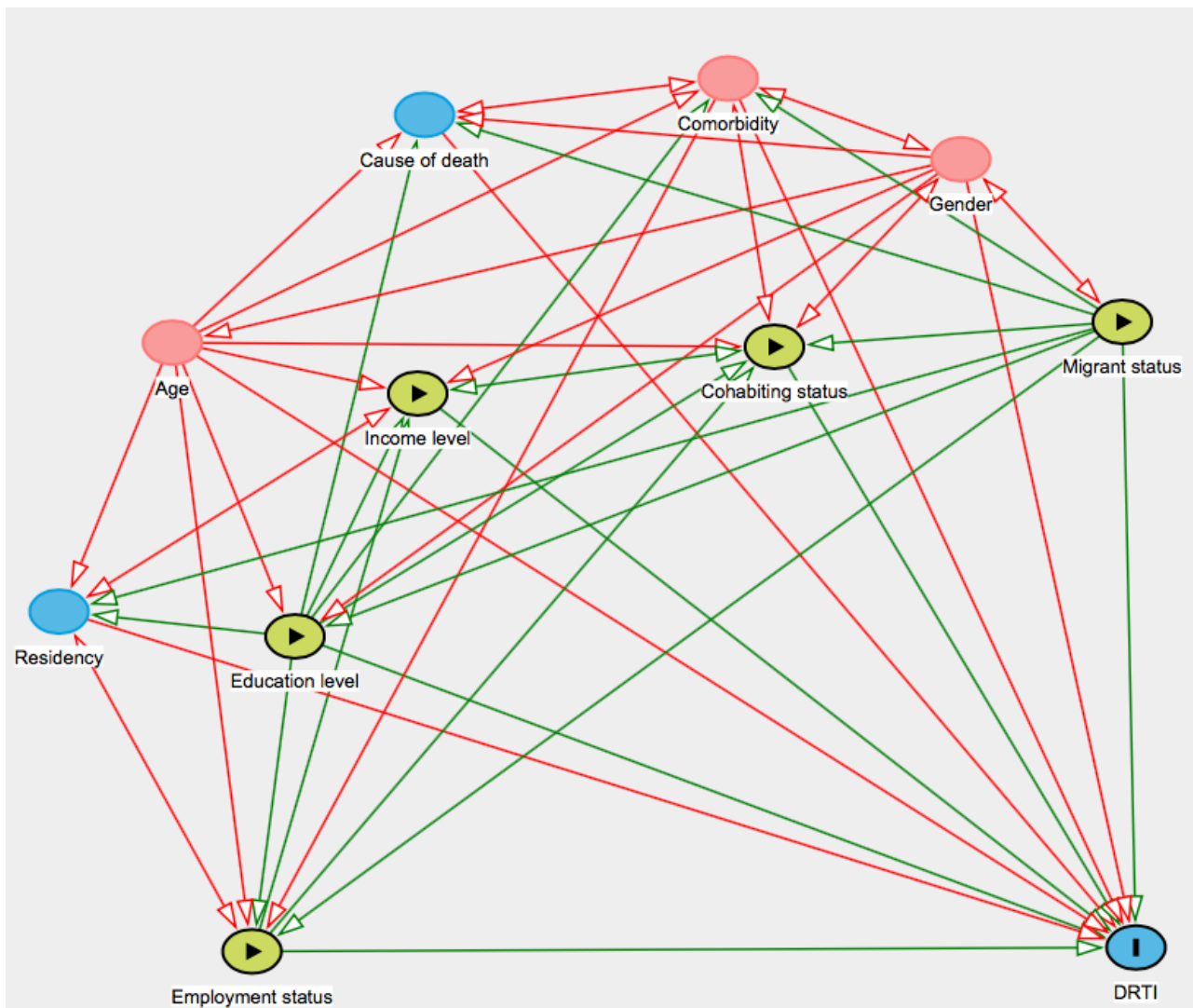
Supplemental figure 2
Directed Acyclic Graph (DAG) showing pathways for included confounders. Green pathways represent causal pathways while red pathways represent biasing pathways.

The crude and adjusted estimates varied markedly, especially in the association between income and cohabiting status. Thus, we repeated the analysis by including only one covariate at a time, and found age and cause of death to have the greatest confounding affect, which emphasises the importance of inclusion of these covariates. Even though, we have included various covariates, there is

still a risk of residual confounding, which is inadequate adjustment for the confounder, and unmeasured confounding, which is remaining or unnoticed confounders.

We did not adjust for hospital admission rates. Hence, we do not know whether patients received DRTI as a part of hospital discharge procedure. Thereby, the discharged patients with DRTI would also be the ones spending their last time at home and redeeming prescription medication at the pharmacies, while patients without DRTI would get medicine provided during their hospital admission (Supplemental figure 3). As a method to eliminate this potential confounding, we made sensitivity analyses restricted to non-hospitalised cancer patients, both while examining the association between socioeconomic position and DRTI and while examining the relation between DRTI and the frequency in redeemed palliative medicine. The findings were similar to the main analyses, suggesting that hospital admission rates did not significantly confound the results.
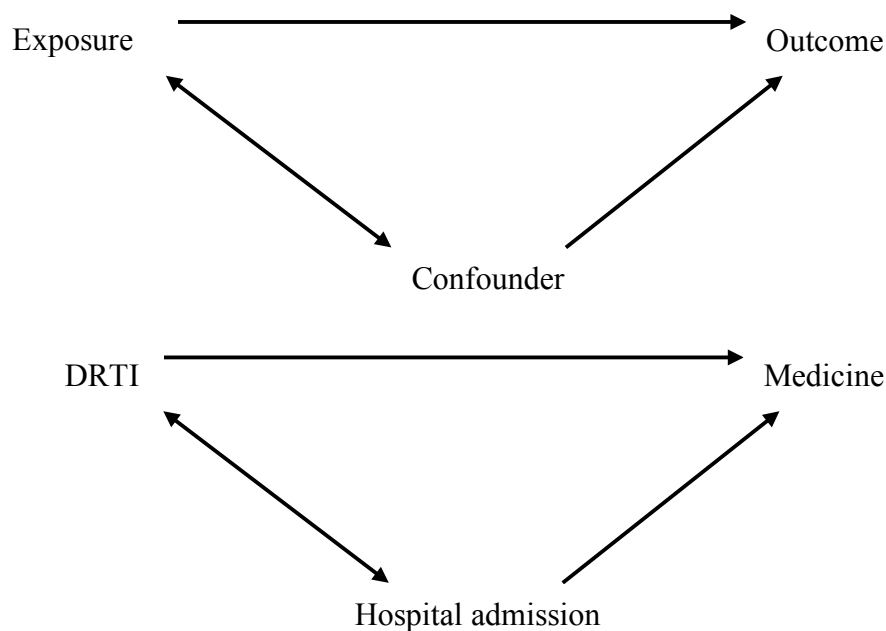
Supplemental Figure 3
a. General correlation between exposure, outcome and confounder.
b. Possible confounding in the present study

Effect modification

Effect modification is whether the presence or absence of a variable changes the effect of exposure on the outcome. [48] Opposite from confounding which we want to eliminate, effect modification is an elaborated description of the effect and important to highlight.

We examined the interaction between education, employment and income by stratifying for each one of them. As presented in Table 4, we found that low educated patients were 1.22 times as likely to receive DRTI if they had a high income compared to low income. This PR was only 1.13 in the high-educated group (Supplemental Figure 4). When we stratified for employment, we found the same pattern. Hence, the results suggest, that if you have a high job position or a high education, income is slightly less associated with the probability of DRTI registration. Consequently, employment and education may be effect modifiers as they affect the association between income and DRTI.
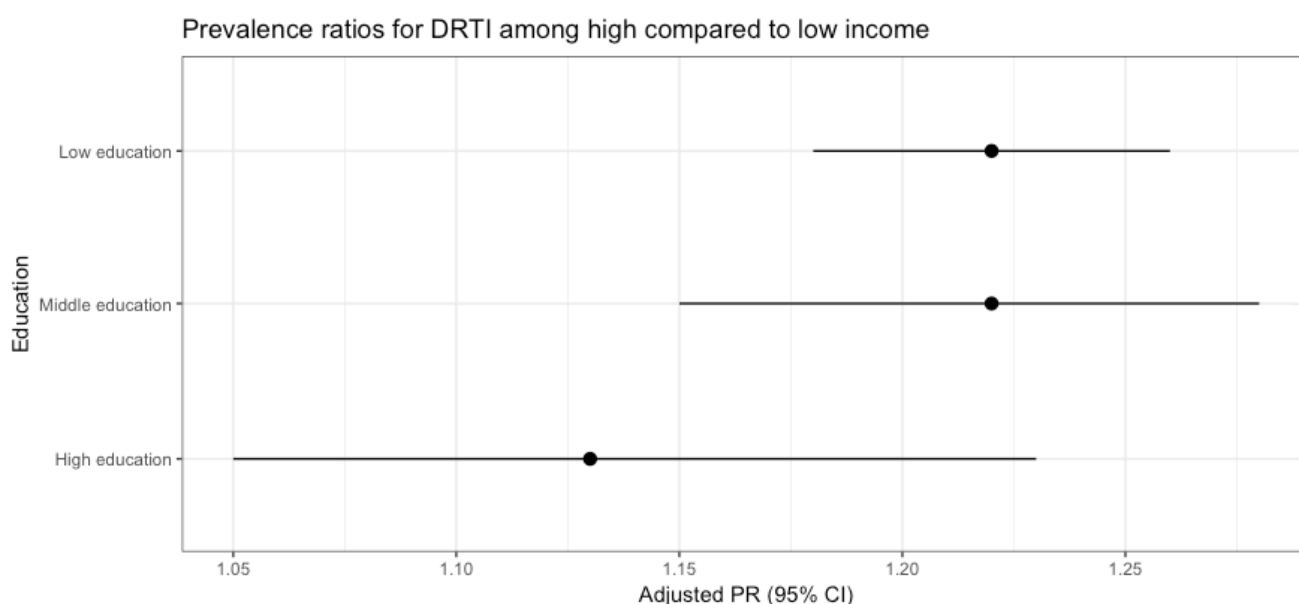
Supplemental Figure 4
Forest plot showing PR stratified by educational level for DRTI for high income compared to low income

When comparing our results to other studies, and as education is a typical marker of socioeconomic position, we found it surprising, that we did not find an association between education and DRTI.

22

Especially, while we found an association in the unadjusted analysis. Consequently, as mentioned, we examined the included covariates and found age and cause of death to have the greatest confounding affect. We wondered if cause of death could be a step in the causal path instead of a confounding variable, e.g., low education increases the risk of life style diseases (non-cancer) which results in low probability of DRTI. Subsequently, we stratified by cause of death by grouping patients into cancer and non-cancer patients (see Table 3). Interestingly, we found the association between socioeconomic factors and DRTI to be more prominent among non-cancer patients. Also, among non-cancer patients we found an association between education and DRTI that was not present among cancer patients. Hence, cause of death may be an effect modifier in the association between education and DRTI and this is a result we want to clarify, not hide in an adjusted analysis. One explanation for these findings may be that health professionals tend to focus on cancer patients while overlooking needs in non-cancer patients. [34,35] Thus, while cancer patients in general are more likely to receive DRTI, it seems that only high educated non-cancer patients receive DRTI.

External validity

External validity describes to which extent the results can be generalised to other situations e.g. to other patients in other countries. In this present study, we included all patients dying from eight illnesses accounting for two thirds of all deaths in Denmark in a period of ten years. Hence, our findings may apply a broad range of terminally ill patients. Conversely, our stratified analysis suggests, the association between socioeconomic position and DRTI to vary across death causes, why generalisation of the overall results to all types of terminally ill patients, should be done with caution. Also, for our results to be useful in different countries, it is important to focus on DRTI as a marker of planned end-of-life care and not a specific Danish drug reimbursement. However, further studies are needed to compare DRTI to other international measures of high quality end-of-life.

Additional results

We found socioeconomic position including high income, living with a partner, being immigrant or descendant of such, and unemployment to be associated with increased probability of DRTI allocation, despite a tax-financed free-access healthcare system.

Additionally, we wanted to examine if the association between socioeconomic factors and DRTI had changed over time. As The Danish Health Authority focusses on minimising the inequality in health in Denmark, we expected to find a decreasing association between socioeconomic position and DRTI. [49] Hence, we repeated the analyses on two study populations; the patients who deceased in 2006-2007 and the patients who deceased in 2014-2015. The results are presented in Supplemental Table 1 and suggest a change in socioeconomic inequality in DRTI status over time. Among the patients who deceased in 2006-2007, 23.8% received DRTI and 96.8% of these were cancer patients. In the period 2014-2015, 32.9% received DRTI and cancer patients accounted for 90.1%. Over time, income and cohabiting status became less associated with DRTI status, while being immigrant or descendant of such became associated with higher likelihood of receiving DRTI. We also found, that in 2006-2007, having an academic or leadership position was associated with highest likelihood of receiving DRTI, while in 2014-2015, being unemployed or pensioner was associated with the highest likelihood of DRTI allocation.

Perspectives and future studies

In the present population-based study, we have demonstrated an association between four specific socioeconomic factors and DRTI status. Also, we have proposed DRTI to be a marker of planned end-of-life care, and we have shown use of palliative medication to differ between patients with and without DRTI. However, additional research is needed on differences in end-of-life care between patients with and without DRTI including hospital admission rates, access to outreach specialist palliative care teams and place of death. Also, efforts are needed to compare DRTI as a marker of

planned end-of-life care with other international measures of high-quality end-of-life care. Nevertheless, our results indicate, that planned end-of-life care is not equally accessible for all patients. Therefore, this study may increase awareness of inequality and thereby help health professionals focus on vulnerable terminally ill patients. Enhanced focus may potentially decrease inequality between patients with high and low socioeconomic position. In addition, we have in this supplemental section displayed a study examining the change in socioeconomic inequality in DRTI status over time. During the study period, we have found an increase in overall proportion of DRTI and a decrease in the association between income level and cohabiting status and DRTI. These results may reflect the Danish Health Authority's initiatives to reduce inequality in health. [49] However, over time, an association between migrant status and DRTI appeared and employment status remained somehow associated with DRTI.

Finally, with this study, we have added to the body of literature documenting variation in end-of-life care, however, efforts are warranted to further understand the mechanisms of variation in a free-access healthcare system by exploring geographical variation in planned end-of-life care. Consequently, we have initiated a second study which aims to examine geographical variation in the use of DRTI among Danish terminally ill patients.

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Tables and figures

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┌─────────────────────────────────────────────────────────┐
│  Patients who died from cancer, dementia, ischemic heart │
│  disease, chronic obstructive lung disease, chronic      │
│  liver disease, congestive heart failure, diabetes,      │
│  stroke in 2006-2015                                     │
│                 n = 314,281                              │
└─────────────────────────────────────────────────────────┘
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Excluded:
Missing data in CRS: 2,446 patients
Missing information on DRTI status or
medicine purchase: 4,647 patients
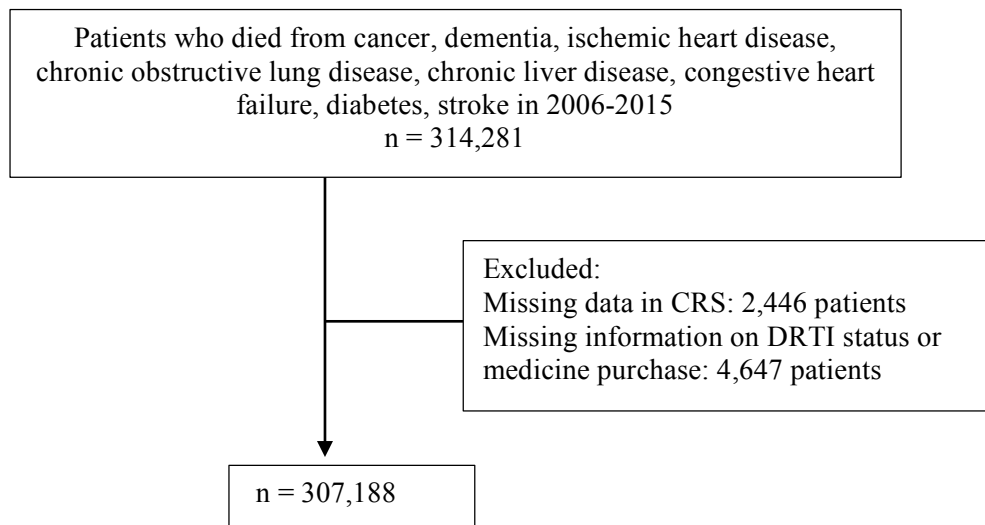
n = 307,188

Figure 1: Flowchart of the study population

Table 1 Characteristics of the study population according to DRTI allocation

	All patients		DRTI allocation		No DRTI allocation	
	No.	%	No.	%	No.	%
Total	307,188	100	85,616	27.9	221,572	72.1
Cause of death						
Cancer	151,246	49.2	80,439	94.0	70,807	32.0
Dementia	30,375	9.9	893	1.0	29,482	13.3
Ischemic heart disease	24,094	7.8	342	0.4	23,752	10.7
Chronic obstructive lung disease	32,699	10.6	1,767	2.1	30,932	14.0
Chronic liver disease	7,391	2.4	341	0.4	7,050	3.2
Congestive heart failure	14,531	4.7	603	0.7	13,928	6.3
Diabetes	13,050	4.3	413	0.5	12,637	5.7
Stroke	33,802	11.0	818	1.0	32,984	14.9
Gender						
Male	150,438	49.0	43,947	51.3	106,491	48.1
Female	156,750	51.0	41,669	48.7	115,081	51.9
Age						
18-69	85,333	27.8	35,742	41.8	49,591	22.4
70-79	82,523	26.9	26,951	31.5	55,572	25.1
80-89	99,450	32.4	19,435	22.7	80,015	36.1
90+	39,882	13.0	3,488	4.1	36,394	16.4
Comorbidity (CCI)						
0	147,492	48.0	45,692	53.4	101,800	45.9
1-2	155,746	37.7	31,275	36.5	84,471	38.12
≥3	43,950	14.3	8,649	10.1	35,301	15.9
Region						
North Denmark Region	34,797	11.3	9,684	11.3	25,113	11.3
Central Denmark Region	65,670	21.4	21,228	24.8	44,442	20.1
Region of Southern Denmark	69,832	22.7	20,583	24.0	49,249	22.2
Capital Region of Denmark	86,620	28.2	20,457	23.9	66,163	29.9

Region Zealand	50,175	16.3	13,630	15.9	36,545	16.5
Unknown	94	0.0	34	0.0	60	0.0
Education level[1]						
Low	138,996	45.3	38,573	45.1	100,423	45.3
Middle	94,397	30.7	31,627	36.9	62,770	28.3
High	29,297	9.5	10,773	12.6	18,524	8.4
Unknown	44,498	14.5	4,643	5.4	39,855	18.0
Income[2]						
Low	100,990	32.9	18,426	21.5	82,564	37.3
Middle	100,991	32.9	25,759	30.1	75,232	34.0
High	100,991	32.9	39,839	46.5	61,152	27.6
Unknown	4,216	1.4	1,592	1.9	2,624	1.2
Cohabiting status						
Living alone	184,831	60.2	37,946	44.3	146,885	66.3
Living with a partner	122,263	39.8	47,636	55.6	74,627	33.7
Unknown	94	0.0	34	0.0	60	0.0
Migrant status						
Non-immigrant	296,886	96.7	82,444	96.3	214,442	96.8
Immigrant or descendant	10,302	3.4	3,172	3.7	7,130	3.2
Employment						
Unemployed, social security, student	13,117	4.3	6,774	7.9	6,343	2.9
Pensioner	270,330	88.0	69,200	80.8	201,130	90.8
Employed	17,954	5.8	7,471	8.7	10,483	4.7
Academic or leadership position	5,705	1.9	2,139	2.5	3,566	1.6
Unknown	82	0.0	32	0.0	50	0.0

[1] Education level: low (International Standard Classification of Education (ISCED) level 0-2), middle (ISCED level 3-4) and high (ISCED level 5-8).

[2] Income: tertiles of mean annual family income during a five-year period before death.

Table 2 Crude and adjusted prevalence ratio (PR) of registration with DRTI according to socioeconomic factors

	DRTI		Unadjusted PR	Adjusted PR[5]	Mutually adjusted PR[6]
	No.[4]	%	PR (95% CI)	PR (95% CI)	PR (95% CI)
Education level[1]					
Low	38,573/ 138,996	27.8	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)
Middle	31,627/ 94,397	33.5	1.21 (1.19-1.22)	1.00 (0.99-1.01)	0.98 (0.97-0.99)
High	10,773/ 29,297	36.8	1.33 (1.30-1.35)	1.02 (1.00-1.04)	0.98 (0.96-1.00)
Income[2]					
Low	18,426/ 100,990	18.3	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)
Middle	25,759/ 100,991	25.5	1.40 (1.37-1.42)	1.16 (1.14-1.20)	1.10 (1.07-1.12)
High	39,839/ 100,991	39.5	2.13 (2.13-2.20)	1.22 (1.17-1.26)	1.13 (1.10-1.17)
Cohabiting status					
Living alone	37,946/ 184,831	20.5	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)
Living with a partner	47,636/ 122,263	39.0	1.90 (1.88-1.92)	1.18 (1.15-1.22)	1.12 (1.09-1.14)
Migrant status					
Non-immigrant	82,444/ 296,886	27.8	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)
Immigrant including descendants	3,172/ 10,302	30.8	1.11 (1.08-1.14)	1.04 (1.01-1.07)	1.08 (1.05-1.11)
Employment					
Unemployed, social security, student	6,774/ 13,117	51.6	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)

Pensioner	69,200/ 270,330	25.6	0.50 (0.49-0.50)	1.01 (0.99-1.03)	0.99 (0.97-1.00)
Employed	7,471/ 17,954	41.6	0.81 (0.79-0.83)	0.86 (0.84-0.87)	0.83 (0.82-0.85)
Academic or leadership position	2,139/ 5,705	37.5	0.73 (0.70-0.75)	1.00 (0.96-1.03)	0.95 (0.93-0.99)
Socioeconomic profile [3]					
"Worst off profile"	72/246	29.3	1.00 (Ref.)	1.00 (Ref.)	
"Best off profile"	56/89	62.9	2.15 (1.67-2.76)	1.36 (1.10-1.67)	

[1] Education level: low (International Standard Classification of Education (ISCED) level 0-2), middle (ISCED level 3-4) and high (ISCED level 5-8).

[2] Income: tertiles of mean annual family income during a five-year period before death.

[3] Data driven: The calculated PRs determines the worst/ best combination of all five socioeconomic factors.

"Worst off profile" (worst combination of socioeconomic factors) if low education, low income, living alone, non-immigrant and employed.

"Best off profile" (best combination of socioeconomic factors) if high education, high income, living with a partner, immigrant or descendant of such and unemployed.

[4] Patient fraction receiving DRTI in each group.

[5] Adjusted for age, gender, cause of death, comorbidity. Clustered within municipality.

[6] Adjusted for age, gender, cause of death, comorbidity, education, income, cohabiting status, migrant status and employment. Clustered within municipality.

Table 3 Crude and adjusted prevalence ratio (PR) of socioeconomic factors according to registration with DRTI – stratified by cause of death

	Cancer			Non-cancer		
	Unadjusted PR	Adjusted PR[3]	Mutually adjusted PR[4]	Unadjusted PR	Adjusted PR[3]	Mutually adjusted PR[4]
	PR (95% CI)	PR (95% CI)	PR (95% CI)	PR (95% CI)	PR (95% CI)	PR (95% CI)
Education level[1]						
Low	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)
Middle	1.03 (1.02-1.04)	0.99 (0.98-1.00)	0.97 (0.96-0.99)	1.07 (1.00-1.13)	1.06 (1.00-1.12)	0.99 (0.94-1.05)
High	1.06 (1.04-1.07)	1.01 (0.99-1.03)	0.98 (0.96-1.00)	1.07 (0.97-1.18)	1.13 (1.03-1.24)	0.97 (0.88-1.07)
Income[2]						
Low	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)
Middle	1.15 (1.14-1.17)	1.12 (1.09-1.15)	1.06 (1.03-1.08)	1.75 (1.63-1.89)	1.64 (1.48-1.80)	1.52 (1.38-1.67)
High	1.29 (1.28-1.31)	1.14 (1.10-1.19)	1.08 (1.04-1.11)	2.10 (1.95-2.26)	1.93 (1.77-2.11)	1.78 (1.63-1.94)
Cohabiting status						
Living alone	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)
Living with a partner	1.22 (1.21-1.23)	1.16 (1.13-1.19)	1.12 (1.09-1.14)	1.51 (1.43-1.60)	1.39 (1.29-1.50)	1.12 (1.04-1.19)
Migrant status						
Non-immigrant	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)
Immigrant including descendants	1.08 (1.05-1.11)	1.04 (1.01-1.07)	1.08 (1.05-1.11)	1.01 (0.87-1.18)	0.98 (0.78-1.22)	1.10 (0.88-1.37)
Employment						

Unemployed, social security, student	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)
Pensioner	0.77 (0.76-0.78)	1.01 (0.99-1.03)	0.99 (0.97-1.01)	1.26 (1.02-1.55)	1.53 (1.23-1.91)	1.30 (1.04-1.63)
Employed	0.82 (0.80-0.84)	0.86 (0.84-0.87)	0.84 (0.82-0.86)	0.48 (0.34-0.66)	0.65 (0.48-0.89)	0.53 (0.40-0.72)
Academic or leadership position	0.83(0.81-0.86)	0.99 (0.96-1.03)	0.96 (0.93-0.99)	1.00 (0.72-1.41)	1.30 (0.88-1.93)	1.06 (0.72-1.56)

[1] Education level: low (International Standard Classification of Education (ISCED) level 0-2), middle (ISCED level 3-4) and high (ISCED level 5-8).

[2] Income: tertiles of mean annual family income during a five-year period before death.

[3] Adjusted for age, gender, comorbidity. Clustered within municipality.

[4] Adjusted for age, gender, comorbidity, education, income, cohabiting status, migrant status and employment. Clustered within municipality.

Table 4 Adjusted[1] prevalence ratio (PR) of registration with DRTI according to income level. Stratified by education and employment

	Low income	Middle income	High income
	PR (95% CI)	PR (95% CI)	PR (95% CI)
All patients	1.00 (Ref.)	1.16 (1.14-1.20)	1.22 (1.17-1.26)
Employment			
Unemployed, social security, student	1.00 (Ref.)	1.13 (1.06-1.21)	1.36 (1.29-1.44)
Pensioner	1.00 (Ref.)	1.16 (1.13-1.20)	1.22 (1.17-1.27)
Employed	1.00 (Ref.)	1.06 (0.93-1.20)	1.16 (1.01-1.34)
Academic or leadership position	1.00 (Ref.)	1.06 (0.94-1.20)	1.08 (0.98-1.20)
Education level[2]			
Low	1.00 (Ref.)	1.15 (1.13-1.18)	1.22 (1.18-1.26)
Middle	1.00 (Ref.)	1.12 (1.07-1.17)	1.22 (1.15-1.28)
High	1.00 (Ref.)	1.08 (1.00-1.16)	1.13 (1.05-1.23)

[1] Adjusted for age, gender, cause of death, comorbidity. Clustered within municipality.

[2] Education level: low (International Standard Classification of Education (ISCED) level 0-2), middle (ISCED level 3-4) and high (ISCED level 5-8).

Table 5 Frequency of number of redeemed prescriptions on palliative medication[1] the last month prior to death[2].

	DRTI	No DRTI
	%	%
All palliative medication		
0	4.5	23.7
1-4	40.4	55.5
5-9	40.1	18.1
10 $\leq$	15.0	2.6
Opioids		
0	9.7	45.4
1-4	56.0	48.8
5 $\leq$	34.4	5.8
Anxiolytics		
0	61.0	74.5
1-4	38.4	25.2
5 $\leq$	0.7	0.3
Sedatives		
0	52.9	81.8
1-4	46.0	18.2
5 $\leq$	1.1	0.1
Antidepressants		
0	74.4	66.4
1-4	25.1	31.7
5 $\leq$	0.4	2.0

[1] Opioids, anxiolytics, sedatives and antidepressants.

[2] The comparison is restricted to 264,075 patients with medicine data recorded in the Register of Medicinal Product Statistics the last month prior to death.

Supplemental Table 1 Crude and adjusted prevalence ratio (PR) of socioeconomic factors according to registration with DRTI – stratified by year of death

	Year of death 2006-2007			Year of death 2014-2015		
	Unadjusted PR	Adjusted PR[3]	Mutually adjusted PR[4]	Unadjusted PR	Adjusted PR[3]	Mutually adjusted PR[4]
	PR (95% CI)	PR (95% CI)	PR (95% CI)	PR (95% CI)	PR (95% CI)	PR (95% CI)
Education level[1]						
Low	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)
Middle	1.15 (1.11-1.19)	0.97 (0.94-0.99)	0.96 (0.93-0.98)	1.20 (1.16-1.24)	0.99 (0.97-1.01)	0.98 (0.96-0.99)
High	1.28 (1.22-1.36)	0.97 (0.94-1.02)	0.96 (0.92-0.99)	1.29 (1.24-1.35)	1.01 (0.98-1.03)	0.98 (0.95-1.01)
Income[2]						
Low	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)
Middle	1.46 (1.39-1.53)	1.13 (1.08-1.18)	1.01 (0.96-1.05)	1.26 (1.22-1.31)	1.07 (1.04-1.10)	1.02 (0.99-1.05)
High	2.35 (2.25-2.46)	1.19 (1.11-1.27)	1.03 (0.97-1.10)	1.84 (1.77-1.90)	1.12 (1.08-1.16)	1.05 (1.00-1.09)
Cohabiting status						
Living alone	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)
Living with a partner	2.05 (1.98-2.12)	1.24 (1.28-1.29)	1.20 (1.16-1.25)	1.74 (1.70-1.79)	1.14 (1.10-1.17)	1.12 (1.08-1.15)
Migrant status						
Non-immigrant	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)
Immigrant including descendants	1.06 (0.97-1.16)	0.98 (0.89-1.08)	1.04 (0.94-1.14)	1.13 (1.06-1.21)	1.07 (1.03-1.11)	1.08 (1.04-1.13)
Employment						

Unemployed, social security, student	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)	1.00 (Ref.)
Pensioner	0.69 (0.63-0.76)	1.26 (1.18-1.36)	1.17 (1.09-1.25)	0.52 (0.49-0.54)	1.00 (0.96-1.03)	1.00 (0.96-1.03)
Employed	1.41 (1.27-1.56)	1.14 (1.07-1.22)	1.07 (1.00-1.14)	0.73 (0.67-0.78)	0.83 (0.80-0.87)	0.83 (0.79-0.86)
Academic or leadership position	1.09 (0.96-1.25)	1.28 (1.17-1.41)	1.17 (1.06-1.28)	0.70 (0.63-0.78)	0.96 (0.89-1.03)	0.94 (0.88-1.02)

[1] Education level: low (International Standard Classification of Education (ISCED) level 0-2), middle (ISCED level 3-4) and high (ISCED level 5-8).

[2] Income: tertiles of mean annual family income during a five-year period before death.

[3] Adjusted for age, gender, comorbidity. Clustered within municipality.

[4] Adjusted for age, gender, comorbidity, education, income, cohabiting status, migrant status and employment. Clustered within municipality.

Reports/PhD theses from Department of Clinical Epidemiology

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