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Geographic and socioeconomic variation in the utilisation of specialist health care services in Norway

Three selected health care services

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Contents

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Abbreviations

AF	Atrial fibrillation
CCI	Charlson comorbidity index
CI	Confidence interval
CPI	Consumer price index
CPP	Cancer Patient Pathways
CRN	Cancer Registry of Norway
CSDH	The Commission on Social Determinants of Health
DAG	Directed acyclic graph
DRG	Diagnoses related groups
EQ	Extremal quotient
GP	General practitioner
HT	Hospital trust
ICD-10	International Statistical Classification of Diseases and Related Health Problems
IRR	Incidence rate ratios
ISCED	International standard classification of education
NCSP	Nomesco Classification of Surgical Procedures
NPR	Norwegian Patient Register
OR	Odds ratio
REK	Regional Committees for Medical and Health Research Ethics
RHA	Regional health authority
SD	Standard deviation
SDH	Social determinants of health
SDM	Shared decision making
SES	Socioeconomic status
SSB	Statistics Norway

List of papers

This thesis is based on the following papers, which hereafter are referred to as paper I, paper II and paper III:

I. Olsen F, Balteskard L, Uleberg B, Jacobsen BK, Heuch I, Moen A. *Impact of parents' education on variation in hospital admissions for children: a population-based cohort study.* BMJ Open. 2021;11:e046656. doi:10.1136/bmjopen-2020-046656

II. Olsen F, Jacobsen BK, Heuch I, Tveit KM, Balteskard L. *Equitable access to Cancer Patient Pathways in Norway - A national registry-based study.* BMC Health Serv Res 21, 1272 (2021). doi:10.1186/s12913-021-07250-1

III. Olsen F, Uleberg B, Jacobsen BK, Heuch I, Tande P, Bugge E, Balteskard L. *Socioeconomic and regional differences in ablation of atrial fibrillation in Norway - a national cohort study.* BMC Public Health 22, 303 (2022). doi:10.1186/s12889-022-12628-9

Summary

The overall theme of this thesis is geographic and socioeconomic variation in the use of specialist health care services. Three different health care services were studied. Complete population data on individual level with high level of quality from nationwide registries (i.e., The Norwegian Patient Registry, The Cancer Registry of Norway and Statistics Norway) were used in the analysis.

The main aims of the thesis were to: 1) explore geographic variation in the use of three different health care services in Norway, 2) explore socioeconomic variation in the use of three different health care services in Norway, and 3) investigate whether geographic variation in the use of these health care services can be explained by differences in socioeconomic status.

In paper I, hospital admissions for children aged 1-16 years were studied. In paper II, cancer patient pathways (CPP) for lung, colorectal, prostate or breast cancer were studied, and the focus was on two different proportions; i) the proportion of patients in cancer patients pathways who do not have the relevant cancer, and ii) the proportion of cancer patients included in cancer patient pathways. In paper III patients with atrial fibrillation and the proportion treated with ablation were studied.

Substantial geographic and socioeconomic variation was documented, and possible differences in socioeconomic status could not explain the geographic variation. Children of parents with low educational level had the highest admission probability, the highest number of admissions, but the reason for the admission tended to be less severe. Cancer patients in high income groups had the highest probability of being included in cancer patient pathways, while for the patients included in the cancer patient pathways, no systematic differences in the proportion of patients who do not have the relevant cancer were found with income and education groups. Atrial fibrillation patients with high level of education and high income were more frequently treated with ablation, and the education effect increased with increasing age.

The variation documented in this thesis challenges the idea that the distribution of medical practice and care in Norway is rational and evidence-based. Differences in capacity can probably explain some of the geographic variation, and differences in need might explain some of the socioeconomic variation. However, in search of explanations one must also study the impact of personal beliefs in both patients and physicians, local traditions, and clinical practice.

Sammendrag

Det overordnede tema for denne avhandlingen er geografisk og sosioøkonomisk variasjon i forbruk av spesialisthelsetjenester. I avhandlingen blir tre forskjellige typer helsetjenester studert. I analysene ble det benyttet komplette populasjonsdata på individnivå, med høy grad av kompletthet og høy kvalitet, fra nasjonale registre (Norsk Pasient Register, Kreftregisteret og Statistisk sentralbyrå).

De overordnede målsettingene i avhandligen var å: 1) utforske geografisk variasjon i forbruket av tre forskjellige helsetjenester i Norge, 2) utforske sosioøkonomisk variasjon i forbruket av tre forskjellige helsetjenester i Norge, og 3) undersøke hvorvidt geografisk variasjon i forbruk av disse helsetjenestene kunne forklares med forskjeller i sosioøkonomisk status.

I artikkel I ble sykehusinnleggelser for barn i alderen 1-16 år studert. I artikkel II ble pakkeforløp for kreft for lunge-, colorectal-, prostata- og brystkreft studert, og det ble fokusert på to forskjellige populasjoner; i) andelen pakkeforløpspasienter som ikke hadde den aktuelle krefttypen, og ii) andelen kreftpasienter som ble inkludert i pakkeforløp. I artikkel III ble atrieflimmerpasienter og andelen som ble behandlet med ablasjon studert.

Betydelig geografisk og sosioøkonomisk variasjon ble funnet, og den geografiske variasjonen kunne ikke forklares med forskjeller i sosioøkonomisk status mellom de geografiske områdene. Barn med foreldre med lavt utdanningsnivå hadde størst sannsynlighet for å bli innlagt og flest innleggelser pr barn, og samtidig de minst alvorlige innleggelsene. Kreftpasienter i den høyeste inntektsgruppen hadde størst sannsynlighet for å bli inkludert i pakkeforløp, mens for andelen pakkeforløpspasienter som ikke hadde den aktuelle krefttypen ble det ikke funnet noen systematiske forskjeller mellom inntekts- og utdanningsgruppene. Atrieflimmerpasienter med høy utdanning og/eller høy inntekt ble oftere behandlet med ablasjon, og utdanningseffekten var sterkere med økende alder.

Variasjonen som er dokumentert i denne avhandlingen utfordrer oppfattelsen om at helsetilbudet og medisinsk praksis i Norge er rasjonell og evidensbasert. Kapasitetsforskjeller kan antagelig forklare deler av den geografiske variasjonen, og forskjeller i behov kan antagelig forklare noe av den sosioøkonomiske variasjonen. For å forstå årsakene til variasjon må man også studere hva som ligger bak kliniske beslutninger, dvs. både pasientenes og legenes preferanser, samt lokale tradisjoner og klinisk praksis.

1 Introduction

Norway has a universal health care system and in-hospital treatment is free of charge. It is a fundamental principle in this system that equal needs should be met by equal services regardless of e.g., socioeconomic status (SES) or place of residence. Universal principles for prioritisation based on benefit, severity and resource use are meant to form the basis for decisions on resource distribution in the health service [1].

However, an increasing number of studies indicate that this principle is not adequately met, in Norway as well as in other Western countries [2–6]. Several decades ago, Wennberg reported on small area variations in health care delivery, which could not be explained by corresponding variations in need [7]. Geographic variation in access to health care in Norway has been documented in a broad spectrum of services [2, 8], and especially by the Norwegian Healthcare Atlases [9].

Several studies report socioeconomic differences in utilisation of health care. For example patients with lower income or education are more frequent users of general practitioner services while relatively wealthy and/or highly educated people visit more specialists and have more access to sophisticated therapies [3–6, 10].

1.1 Geographic variation in health care utilisation

Analyses of variation in the population's use of health services between geographical areas are referred to as the research field "small-area-variation" [7]. As early as 1938, a study was published that showed large geographic differences for tonsillectomy among English school children. Both surgeons' practices and socio-economic conditions contributed to the differences [11]. In the late 1960s, Wennberg and Gittelsohn designed the "small area analysis" method to compare population-based rates of care among neighbouring hospital service areas in Vermont to study whether all the residents received the health services they were entitled to [12]. The resource input and the health service utilisation among populations living within the geographic boundaries of the hospital referral areas, were studied. The hospital referral areas of Vermont were remarkably similar on the demand side, with comparable insurance coverage, educational level, economic circumstances, and ethnic background. However, the per capita number of hospital beds, hospital personnel, and physicians varied over 50% across the hospital referral areas. Unexpectedly large variations between the areas in the use of almost all kinds of health resources were found, including personnel and expenses [7]. They also found huge variation between nearby areas in the rates of surgical procedures such

as appendectomy (four-fold), tonsillectomy (twelve-fold) and several other procedures. There was considerabily variation between neighbouring areas just a few blocks apart, the variations were not explained by illness, poverty or ethnicity. An important feature of "small-area-analysis" is that it is population-based [12]. Wennberg and Gittelsohn found substantial differences in rates of utilisation of health care between demographically similar populations. Wennberg concludes that it was not the rate at which they got sick and went to the doctor that varied, but it was what happened after patients met with their physicians [12]. Substantial variation in the use of health services has since the 1970s been reported between countries [13, 14], between regions in countries [15–17] and between areas in regions [18].

Studying variation in the population's use of health services is a method for examining whether the health services are evenly distributed and whether key objectives in health policy are met. There is, to a certain extent, an intended division of work between hospitals, and therefore there may be a substantial difference in the case-mix of patients between the hospitals. In a population-based analysis, the use of health services in groups of patients living within defined geographic areas are compared, regardless of where the population accessed the services. By applying population-based analysis, the impact of this type of case-mix is eliminated, although possible differences in age, gender, and morbidity between the geographical areas that the hospitals serve may still be important.

1.2 Social inequality in health

In countries at all levels of income, health and illness follow a social gradient: the lower the socioeconomic position or status, the worse the health [19, 20]. Socioeconomic status (SES) is the social standing or class of an individual or group, and it is often measured as a combination of education, income and occupation.

Norway is among the countries with the least income inequalities in the world. However, income inequalities have increased in Norway in the past decades [21]. Social inequalities in health in Norway are actually larger in Norway than in many comparable European countries [22, 23]. Norwegians with higher education levels and a good financial situation live longer and have fewer health problems than Norwegians with lower education and poorer economy. Social inequalities in Norway are found at county and municipal level [23]. Those with the highest education live 5-7 years longer and have better health than those with the lowest education [24]. Within the capital (Oslo), life expectancy varies by up to eight years between districts [23]. However, a Norwegian study on income inequality and mortality found that the infant mortality in Norway has greatly declined during the last 70 years,

and that the infant mortality gap between the rich and the poor is levelled out in Norway, both at municipality level and at individual level [25].

In 2005, The Commission on Social Determinants of Health (CSDH) was created by the World Health Organisation (WHO) to promote greater health equity. It focused on structural determinants of health inequities: the social factors that cause unfair, avoidable health differences among population groups [26]. The social determinants of health (SDH) are by the World Health Organization defined as the non-medical factors that influence health outcomes [19]. The determinants are the conditions in which people are born, grow, work, live, and the wider set of forces and systems influencing daily life. These forces and systems include political and economic policies and systems and social norms and policies. Examples of social determinants of health include; income and social protection, education, unemployment and job insecurity, working life conditions, food, insecurity, housing and basic amenities, the environment, early childhood development, social inclusion and non-discrimination, structural conflict, and access to affordable health services of decent quality. The reports from the CSDH affirmed that the fundamental drivers of SDH are the unequal distribution of power, money and resources [27].

1.3 Socioeconomic variation in health care utilisation

Discussions on variation in health care have often been focused on geographic variation, however, the term can also be used to describe differences in health care utilisation according to SES. A wide range of studies has documented associations between SES and utilisation of health care services, both in universal and non-universal health care systems [28–35].

Variation in health care utilisation between SES groups may reflect differences in disease prevalence or need due to lifestyle or environmental factors, but may also be related to other factors, such as doctor-patient communication [36–38]. There is much research on socioeconomic status and health and health care utilisation and this section is not intended to cover the entire field of research. The common explanation for the associations between SES and utilisation of health care services mainly follows four pathways.

Firstly, variation between SES groups may reflect differences in disease prevalence or need due to lifestyle or environmental factors, i.e., the socioeconomic gradient in health [39]. Those with higher education levels and a good financial situation live longer and have fewer health problems than those with lower education and poorer economy. There are substantial social inequalities in health in

Norway, especially between educational groups. As noted above, the relative differences in mortality between education groups in Norway are among the largest in Europe [22, 23, 40].

The second pathway may be related to health literacy and how people in higher SES are more able to navigate within the health care system [41]. Health literacy is the degree to which individuals have the ability to find, understand, and use information and services to inform health-related decisions and actions for themselves and others [42]. Health literate patients may be more capable of understanding, questioning and discussing treatment options with their physician.

The third pathway may be related to how health professionals communicate with patients of different SES. Patients' willingness to participate in shared decision-making may reflect the physician's consulting and communication style. In a meta-analysis regarding doctor-patient communication related to SES, physicians gave more information, more explanations, were more emotionally supportive and more often adapted shared decision making with patients of high SES [36]. Further, patients with low SES received more physical examinations [36].

The fourth pathway is related to the ability to pay for services. Out-of-pocket payment or lack of health insurance may be an obstacle to disadvantaged groups seeking health care. Several studies have demonstrated patient charges as an obstacle [43–45]. In a survey on social inequalities in health service utilisation in Norway by Statistics Norway most people reported that they received adequate health services [46]. Norway has a universal health care system and in-hospital treatment is free of charge. This most likely excludes a significant effect of economic restraints on access to hospital health care in Norway. Most hospital health services in Norway are provided by public hospitals or private hospitals as subcontractors for the public health care system. However, for some health care services, e.g., cosmetic surgery, private health insurance and out-of-pocket payment for private health services may have some impact.

Even though socioeconomic gradients in health care use are found in many studies, the sign of the gradient varies, and there seems to be an association between the sign of the gradient and the degree of specialisation of the service. In health care services with low level of specialisation a negative SES gradient is found [4, 10], while in services with higher degree of specialisation a positive SES gradient is found [47, 48].

1.4 Warranted or unwarranted variation

There are different perceptions of how variation in the use of health services arises and in what way it should be measured and interpreted [49–53]. Variation is often described as being either 'warranted' or 'unwarranted'. Not all variation in healthcare is unwarranted – some is inevitable, some is random and some we have no control over. Variation can be an outcome of innovation, as new solutions and models are being introduced. This type of variation, which is expected and normal, is therefore called warranted.

The other type of variation, which needs to be considered separately and is more challenging, is unwarranted variation. Unwarranted variation in health care service delivery refers to differences that cannot be explained by personal preference, illness, medical need, or the dictates of evidence-based medicine [12]. Unwarranted variation can reveal overuse, underuse and inequity in health care service delivery. Overuse occurs when a service is provided even though its risk of harm exceeds its likely benefit, or when the service is without benefit. Underuse occurs when a service is not provided even though its benefits exceed its likely risk of harm. Inequity of care occurs when parts of the population are not accessing the treatment to the extent that they need.

To understand unwarranted variation in the use of health services, it is natural to take the observed variation as a starting point (Figure 1). The observed variation can be divided into two components; random and systematic variation. The random variation is particularly relevant in the case of analyses of areas with small populations or low volume health services. Such random variation is natural and expected. Some of the systematic variation is due to case-mix, the case-mix is differences in morbidity and in the age and gender composition between the populations of interest. The differences in age and gender composition can easily be adjusted for, and most health care atlases adjust for case-mix by presenting the results as age- and gender adjusted rates, while differences in morbidity and severity are harder to reveal. The remaining part of the systematic variation consists of warranted and unwarranted variation.

Wennberg defined three categories of care for the causes of, and the remedies for, unwarranted variation in [12]; i) effective or necessary care, ii) preference-sensitive care and iii) supply-sensitive care.

Effective care comprises evidence-based interventions where the benefits are thought to exceed the disadvantages, and thus should be offered to all patients in need. For effective care, treatment rates should approach the actual prevalence of the condition, and unwarranted variation is generally due to underuse.

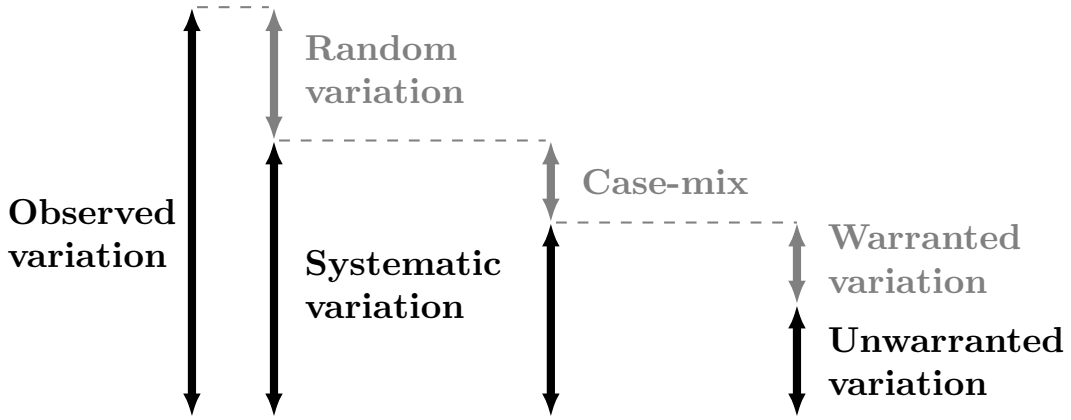

Figure 1: Illustration of variation components.

Preference-sensitive care comprises tests and treatment procedures for conditions for which there is more than one clinically appropriate treatment option. Preference-sensitive care represents health care with alternative treatment options where indications and benefits may be poorly documented or controversial, and may reflect preferences and beliefs of a single physician or department rather than a clear evidence-based approach. Patients should be treated according to their preferences in a clinical environment that supports shared decision making and encourages patients in the choice of treatment [51]. Unwarranted variation in preference-sensitive care is often due to differences in professional opinions or patients' participation in decisions about care. Under the informed patient choice normative standard, the choice of treatment should depend on the patient's preferences [12].

Supply-sensitive care comprises services such as physician visits, referrals, hospitalisations and stays in intensive care units for patients with acute and chronic medical (non-surgical) conditions where the frequency of use is closely associated with the supply of available resources. Unwarranted variation in supply-sensitive care refers to medical services for which utilisation rates are sensitive to local availability of health care resources such as hospital beds, physicians, outpatient capacity, test capacity, and intensive care capacity. When capacity increase, more patients will be treated until the new maximum capacity is reached without necessarily benefiting the patient or the populations' health condition.

Wennberg estimates that effective care accounts for 10-15% of the activity in the Medicare health services in the US, while preference-sensitive and supply-sensitive care accounts for 25% and 60 %, respectively [12].

With the exception of effective care, observing variation cannot by itself define the "right" level of health care service utilisation. According to Goodman, the "right" level depends on the category of care [54]; The right level in effective care is treatment rates similar to the prevalence, and deviation from near 100% reflects less than ideal health system performance. There is no single "right" rate in preference-sensitive care, as the "right" rate reflects the decisions of fully informed patients, while variation in rates reflects both local practice and the influence of clinicians on the patients' decisions. In supply-sensitive care, the "right" rate is generally the lowest rate with comparable outcomes, while higher rates reflect overuse and lower rates reflect underuse.

Sutherland et al. define unwarranted clinical variation as patient care that differs in ways that are not a direct and proportionate response to available evidence, or to the health care needs and informed choices of patients [53]. Sutherland et al. further describes situations where the variation can be either warranted or unwarranted.

The variation can be characterised as warranted when clinical decisions are tailored to the need of patients, based on unbiased discussions and informed consent, and evidence-based recommendations are followed. In addition, the variation can be warranted and interpreted as a reflection of adoption, as there might be differences in skills or resources available between the health care providers.

The variation can be characterised as unwarranted when insufficient information is provided to the patients or when decisions are based on non-clinically relevant patient characteristics (age, gender, SES, ethnicity). The variation is also unwarranted when clinical practice clearly deviates from the available evidence base, due to the providers' needs and preferences or lack of adoption of the evidence-based guidance. Unwarranted variation can also occur if a procedure or treatment is used in other patient groups than those where it was shown to be valuable. Lack of technical acumen, i.e., differences in training, competency, and technical proficiency of providers or limitations in clinicians' ability to resolve uncertainty can also cause unwarranted variation. Finally, the variation can be characterised as unwarranted if allocative decisions and organisational design, resulting in some clinicians' being unable to provide certain elements of care because of resource constraints.

1.5 Factors influencing variation in health care utilisation

What are the driving factors of geographic variation? It is common to divide possible driving factors into supply side and demand side factors. Supply side factors include access to care, medical practice, and provider characteristics. Demand factors are such as health status, demographic and

socioeconomic status. The supply side factors are properties of the health care service and are measured on an aggregate level, while the demand side factors are properties of the individual patients and therefore factors on an individual level. However, as data on individual level often is lacking, the majority of studies apply aggregated measures also for demand side factors.

Although there are numerous studies demonstrating geographic variation, studies on the driving forces of variation are limited [55, 56]. The empirical evidence on whether the demand side or the supply side is the driving force for geographic variation is unclear [56, 57]. Studies from the US found that 40–50% of this variation is attributable to patient demand factors, while the rest is explained by supply factors [58, 59]. A Norwegian study, using migration data to decompose regional variation also found that the supply and demand side each roughly explains half of the variation in health care utilisation [57]. However, the majority of studies concludes that geographic variation is mainly driven by the supply side [49].

According to the definition of unwarranted clinical variation in Sutherland et al., demand side factors are factors influencing or representing health care needs and choices of informed patients. Supply side factors are deviations from the evidence base by physicians or at the organisational level. It is difficult to separately estimate the impact of physicians and patient preferences and other factors because it is difficult to identify factors that affect only supply or demand [49]. Both Finkelstein and Godøy address this by studying migration [57, 59], however they are not able to distinguish between the different supply side factors or between the different demand side factors. Cutler et al. use 'strategic' survey questions of physicians and patients, and find that differences in physician beliefs about efficacy of particular therapies is the most important factor of variation [49].

Most attempts to explore the multiple factors that drive variation have used an ecological approach, analysing aggregated measures such as disease prevalence, average income, average education level or area level deprivation or racial composition of the population. Interpretation of such analyses can be limited because they may be subject to the "ecological fallacy" by inferring risk factors for individuals based on aggregated information.

In the Vermont study, Wennberg and Gittelsohn concluded that the geographic variations were not explained by demand side factors such as illness or SES [12]. Still, many studies investigate whether differences in SES can explain the geographic variation. Most studies on geographic variation controlling for socioeconomic status use ecological or area-level SES measures. A study by Kravdal et al. on all deaths among persons aged 60-89 in Norway showed that 70-80% of the geographic variation

in mortality between municipalities in the period 2000-2008 could be explained by socioeconomic factors [60]. Kravdal et al. found, however, that when applying individual level socio-demographic characteristics, the geographical variation could not be explained. Thus, the explanation was solely due to aggregate-level effects [60]. Kinge et al. found, in a study using SES at municipality level, that about 50% of the variation in obesity between the municipalities in people at 17 years of age in Norway could be explained by SES [61].

In a study with more than 3.5 million individuals in the US, Moss et al. compared the use of individual- and area-level SES when estimating mortality disparities [62]. They found that the validity of area-level indicators was questionable and considerable misclassification was seen.

1.6 The Norwegian health care system

The Norwegian health care system is universal and mainly tax-funded [63]. Equal access to health care of good quality for all inhabitants, regardless of area of residence or socioeconomic background is an overriding principle in national health policy and embedded in health care legislation. The goal of ensuring "equal access to health care of good quality" is explicitly stated in the 1999 Patients' Rights Act. Health care resources should be distributed according to the national principles for priority setting [64].

The central government is responsible for specialist care, which is delivered through four regional health authorities (RHAs). The Ministry of Health and Care Services is responsible for the regulation and supervision of the system and ensures that health and social services are provided in accordance with national legislation and regulations. The Ministry controls the activities in the specialist care through budgets and assignment documents (annual assignment letter of instruction to RHAs).

The four RHAs, each owning several hospital trusts (HTs) with hospitals of varying size and level of expertise, are responsible for providing specialised secondary care. The HTs provide specialist services to the population living within their hospital referral area on behalf of the RHAs. The municipalities are responsible for providing primary care, including GP, out-of-hour services, nursing homes and home care. Patients can choose their GP. Access to specialist health care in Norway is based on referral from a GP. GPs act as gatekeepers. Patients with a referral to inpatient care have a freedom of choice among public and private hospitals that are approved by the Directorate of Health. In 2015 freedom of choice of hospital was extended to any hospital in the EU/ECC, although transportation costs are not covered. According to the Patients' Rights Act, patients are entitled to participate in the

decisions around their health care. This includes the right to participate in choosing between available and medically sound methods of examination and treatment. In the annual assignment letter from the government to the RHAs in 2015/2016, both increased focus on shared decision making and reduction of unwarranted variation were included as specific measures.

The specialised health care system in Norway is publicly financed by a combination of government block grants and activity-based reimbursement to the RHAs. The block grants are risk-adjusted and population-based or 'per capita' financing. The proportion of block grants and activity-based financing has varied. Currently, it is 50/50. Private health insurance is negligible in health care financing, and is mostly a route for quicker access. Private health insurance accounted for less than 1% of the total spending on health in Norway in 2017, and it covered less than 5% of elective services [63]. However, the market for private health insurance in Norway is growing, the number of people with private health insurance more than doubled from 2012 to 2016 (from 225 000 to 500 000 subjects) [63].

All residents of Norway are entitled to essential medical and care services. Inpatient care, day-care and same-day surgery are free of charge. There is co-payment for outpatient specialist visits and prescriptions, radiology and laboratory tests, GP visits, rehabilitation and physiotherapy. In 2022, the annual cap on co-payment was NOK 2921.

1.7 "Variation" in health policy and management

From 2014 and onward, geographic variation has been systematically investigated by the Norwegian Health Care Atlases, a series of reports and online maps on the use of health care services published by the Center for Clinical Documentation and Evaluation (SKDE) and Helse Førde HF [9]. The first report on day surgery was published in 2015, and by date 11 Norwegian Healthcare Atlases have been published. The majority of the atlases have revealed substantial geographic variation.

Since 2015, the Ministry of Health and Care Services has been focusing on unwarranted variation, and in the annual letters of instruction from the government to the RHAs both in 2016 and 2017 the RHAs were asked to use the knowledge of unwarranted variation in their management of the health trusts. The RHAs are instructed to follow up the examples of unwarranted variation revealed in the health care atlases.

In 2016, a white paper called "Priority setting in the health care sector" was published. The Ministry of Health and Care Services states that unwarranted variation in utilisation of health care services is challenging the principle of equality and that it can reflect underuse, overuse or malpractice [1]. In

the recommendation from the Health and Care Committee of the Norwegian parliament (Stortinget) on the National Health and Hospital Plan in 2016, the committee states that substantial geographic differences in utilisation of health care services may be an indication of system failure and can pose a threat to patient safety [65]. The committee points out that standardisation by patient pathways, similar to the model of cancer patient pathways, can be important to ensure predictability, quality and completeness in the supply of health care services.

One of the purposes of the Specialist Health Service Act is to ensure optimal resource utilisation. In addition, according to the Health Personnel Act, the RHAs are obligated to organise the service in a manner that ensures appropriate resource utilisation, this also applies when prioritising among patients, as well as in the diagnosis, treatment and follow-up of the individual patient. In the bill and draft resolution for the budget year 2017 from the Ministry of Health and Care Services, the RHAs and the clinicians are instructed to, based on the health care atlases, to review the services offered with the intent of establishing good practice and resource utilisation and reduce unwarranted variation [66].

In 2019, the Office of the Auditor General of Norway published a report on reasons for variation in utilisation of health care services in Norway [67]. Results from the Norwegian health care atlases are the basis for the report, and especially the results from the Day Surgery Atlas [68] and the Child Healthcare Atlas [69]. Both the Auditor General report and the Health and Care Committee highlight national guidelines as an important tool to promote common understanding and practice [65, 67]. Also, the Directorate of Health emphasises the development of guidelines, standardised clinical pathways, description of procedures, and priority guides as key instruments to ensure common practice and reduce unwarranted variation. In Norway, standardised clinical pathways have been implemented for cancer, stroke, and psychiatry.

1.8 Introduction to the three health care services studied

In a universal health care system with a goal of equality in the services, the present thesis explored the variation in use of three selected specialist health care services in Norway.

The topic for Paper I was medical admissions for Norwegian children, i.e., a large and relatively homogeneous group not significantly affected by lifestyle diseases, and with free access to both primary and specialist care. In paper II, we studied patients within a new organisational framework aiming to improve quality of cancer care and reduce non-medical delay; cancer patient pathways

(CPP). Whereas in paper III, we focused on a health care service in the process of introducing a new treatment procedure; ablation in the treatment of atrial fibrillation.

These three health care services represent a range of the specialised health care services in Norway. The services studied differ in the degree of specialisation, where ablation of atrial fibrillation can be characterised as the most sophisticated or the most specialised service, and Cancer Patient Pathways represent more specialised services than medical admissions of children.

1.8.1 Hospital admissions for children

Norwegian children are among the healthiest in the world. Child mortality (the number of children who die before the age of 5 years) was 2.5 per 1000 live births in 2018 compared to 6.5 in the US [70].

Health care services for children in Norway are provided by different categories of healthcare professionals. All health care for children under the age of 16 is free of charge. Parents who care for sick children (hospitalised or not) are entitled to sick-leave allowance in order to care for sick children (20 days per year for parents with one or two children under 12 years, 30 days for parents with three children under 12 years). Parents are economically compensated for the loss of income if admitted to hospital with their child.

Geographic variation in health care utilisation for children has been described both in publicly financed and privately financed healthcare systems [69, 71, 72]. The Norwegian child health care atlas published in 2015 [69] and the Neonatal health care atlas [73] published in 2016 found relatively large geographic variation between hospital referral areas in admission rates and rates of treatment procedures.

1.8.2 Cancer patient pathways

Cancer patient pathways (CPP) have been established in several countries to avoid an undesirable delay in cancer diagnosis and treatment. In the early 2000s, urgent referral pathways were introduced in the UK and in Spain, targeting an upper limit of two weeks between seeing a GP to being referred to a specialist at a hospital [74, 75]. Denmark implemented CPPs in 2007–2008 [76, 77], and Sweden during the years 2015-2018 [78]. In addition to reducing and standardising waiting times, in Denmark CPPs were also intended to improve survival of cancer patients.

In 2014, the Norwegian Directorate of Health was commissioned by the Ministry of Health and Care Services to prepare pathways for cancer patients. The aim was to reduce unnecessary non-

medical delay in the diagnostic and start of treatment period and to increase satisfaction, quality and predictability for patients with a suspicion of cancer [79]. The RHAs and the HTs were instructed to implement the first cancer patient pathways during 2015. The Norwegian Directorate of Health was assigned a coordinating role in the implementation process. The implementation should be a gradual process, and a step-by-step implementation of the pathways was to be carried out.

Pathways are standardised care processes that cover the entire process, from referral to the specialist health care service and to follow-ups and controls. In the cancer patient pathways, there are differentiated and recommended process times for each cancer pathway. The process times indicate the time between the individual elements in a pathway, e.g., the time from the referral is received in the specialist health service to the time of the first contact at the investigative department. The process times are determined based on reasonable waiting times between the various steps in the process [80].

Norway introduced CPPs in January 2015 for lung, colorectal, breast and prostate cancers [81–84]. Later in 2015, another 24 CPPs were implemented. All Norwegian CPPs were based upon Norwegian guidelines for diagnosis, treatment, and follow-up of the specific cancer groups [85].

Patients are referred to a CPP by a GP, a specialist in private practice or a specialist in a public hospital if the doctor has a "justified suspicion of cancer" [85]. The suspected cancer diagnosis should be based on a set of symptoms and tests, described in national guidelines for CPPs [81–84], and the referral should be labelled as "cancer patient pathway". In Norway, it is a national aim that at least 70% of all cancer patients are included in a CPP [86].

1.8.3 Atrial fibrillation and ablation

Atrial fibrillation (AF) is the most common cardiac arrhythmia, with significant influence on quality of life, morbidity and mortality [87–92]. The prevalence of AF has been increasing over the last decades and is expected to increase further over the next 30 to 50 years [88, 93–96]. Thus, AF has become an important public health issue and a significant contributor to health care costs in the Western world.

Over the last two decades, catheter ablation has evolved as an important treatment option for many patients with symptomatic AF, with reasonable success rates, low complication rates and acceptable cost-effectiveness [89, 91, 97]. The procedure was primarily indicated for patients with non-coronary cardiovascular disease, where rhythm control is the strategy of choice and in whom medical therapy

has failed [90]. However, more recently, catheter ablation has also increasingly been considered as first-line therapy in selected individuals [89, 92, 98, 99].

In 2010 the Norwegian Ministry of Health and Care Services instructed the regional health authorities (RHA) to increase the capacity for catheter ablation of AF, as there was an increasing discrepancy between demand and capacity for catheter ablation in Norway. This led to a substantial increase in the number of radiofrequency ablation procedures performed within the national health care system. In total, 23 159 ablations procedures were performed on 17 909 patients in Norway in the period 2008-2017. The annual number of ablations increased in the period, with a marked increase of 65% from 2010 to 2011. By 2013, Norway was near the top in Europe in number of AF ablations performed per capita [100].

In Norway, only five hospitals perform AF ablations, one in each of the four RHAs. In addition, one private hospital in the South-East RHA performs the procedure as a subcontractor for the regional health authority.

2 Aims of the thesis

Based on linked data from population-based registries, on individual level, the overall aim of this thesis was to generate more knowledge about and explanations of variation in the utilisation of three different health care services in Norway. The aims of the thesis were:

- To explore geographic variation in the utilisation of these health care services.
- To explore socioeconomic variation in the utilisation of these health care services.
- To investigate whether geographic variation in the utilisation of these health care services can be explained by differences in socioeconomic status, using data from individuals.

3 Methods

3.1 Data sources and variables

The study populations were defined using combined data from the Norwegian Patient Register (NPR) and Statistics Norway (SSB), and in paper II also the Cancer Registry of Norway (CRN). Data were linked by an encrypted serial number derived from the unique 11-digit personal identifier held by all persons living in Norway.

3.1.1 The Norwegian Patient Registry (NPR)

The NPR data consisted of patient characteristics (residential information, age and gender), start and end date for the contact, type of contact, hospital, diagnoses, and procedures. All Norwegian hospitals, and all private specialists with public funding contracts, must submit data to NPR for registration and reimbursement purposes.

3.1.2 Statistics Norway (SSB)

In paper I, the data from SSB consisted of, updated for each year, parental level of education, number and birth year of siblings, year of birth of the parents, gender and year of birth and residential municipality, for all Norwegian children aged 1 to 16 years in the period 2008-2016. In paper II and III, the data from SSB consisted of yearly income and educational data, in addition to gender, year of birth, date of death, date of emigration and residential municipality. In paper II the study period was 2015 to 2017, while in paper III the study period was 2008 to 2017.

3.1.3 The Cancer Registry of Norway (CRN)

The data from CRN consisted of cancer diagnosis and date of diagnosis. All Norwegian cancer cases are to be reported to CRN. CRN data were only used in paper II.

3.1.4 Variables common in the papers

Education level was coded applying the international standard classification of education (ISCED) [101]. Higher numbers represented higher education levels; 0 represented less than primary education, and 8 indicated a doctorate or equivalent while 9 was not classified and regarded as missing. Education level in the analyses was recoded into three categories; low (0-2), medium (3-5) and high (6-8), where 3-5 is high school level. In paper I education level was parental education level.

After-tax income was calculated as total income minus assessed tax and negative transfers, with total income representing the sum of income as employee, income from self-employment, property income, capital income and transfers received. The after-tax income was index-adjusted to 2015 by the consumer price index (CPI) to account for inflation. From after-tax income a categorical income variable was defined with three categories; low (less than NOK 240 000), medium (NOK 240 000 - 400 000), high (more than NOK 400 000). Income data were not available in paper 1.

The patients' hospital referral area was defined by place of residence and the corresponding geographical catchments areas served by the 21 Norwegian hospital trusts (HT). In paper 1 the hospital trust's paediatric departments are used for defining hospital referral areas, and therefore 18 hospital referral areas are defined in paper 1. Patients residing in the Helgeland region, who otherwise belong to Helgelandssykehuset hospital trust's catchment area, have been included in the catchment area of Nordlandssykehuset hospital trust, which is responsible for these children. Similarly, the catchment areas of Lovisenberg Diaconal Hospital and Diakonhjemmet Hospital in Oslo are included in the hospital trust's catchment area of Oslo University Hospital. The patients' regional referral area was defined by the catchment areas for the four regional health authorities (RHA) (North, Central, West and South-East) in Norway.

3.1.5 Analytical tools

Data in the three papers were analysed using SAS 9.4 (SAS Institute, Cary NC).

3.2 Paper I - Hospital admissions for children

3.2.1 Study population and data sources

The study population was defined using combined data from the Norwegian Patient Register (NPR) and Statistics Norway (SSB) and included the complete cohort of all Norwegian children aged 1-16 years from 1 January 2008 to 31 December 2016.

3.2.2 Definitions and variables

Hospital admissions for medical diagnoses (non-surgical DRG grouping) of at least one day were included in the analysis. In addition, admissions with certain primary diagnosis not considered paediatric medicine were excluded (for a detailed list of diagnoses, see supplementary material of the publication). Admission episodes with less than eight hours between department stays were considered

as one admission. If an admission consisted of two or more department stays, it was registered as medical if all were registered with a medical diagnosis. Admissions were registered by the year of discharge. In addition, four sub-samples of admissions with gastroenteritis, viral and bacterial infections, epilepsy and asthma were defined by primary and secondary diagnoses (for details, see supplementary of the publication).

The number of siblings was computed each year and analysed as a dichotomous variable; only child or child with siblings.

3.2.3 Statistical analysis

The data were structured as one record per child per year, and the variables were time-dependent.

Age- and gender-adjusted admission rates were calculated for children with medical admissions in the hospital referral areas corresponding to the geographic areas served by the 18 Norwegian hospital trusts. The direct method of standardisation was applied, with three age groups (1-3, 4-9 and 10-16 years). Both annual and overall rates for the period 2008 to 2016 were calculated separately for parents' educational level categories. The reference population was the annual average of all children aged 1 to 16 years in Norway in the period.

Independent variables included were: Child's age and gender, maternal age, maternal and paternal level of education (categorical) and being an only child or not. Due to the high correlation between parents' ages, father's age was not included in the analysis. Restricted cubic splines (4 knots) for age with an interaction terms for gender were applied, to adjust for child's age and gender. High level of education and only child were set as reference categories. In any particular analysis, observations with relevant missing data were excluded.

Admission was a dichotomous variable for each child, and the year of the first admission was used as time of admission. For children with multiple admissions, only the year of the first admission was considered. Admission or not was analysed using discrete-time survival analysis (based on binary logistic regression) [102].

In the analysis of the number of admissions, and the cost or severity of the admission, the study population was restricted to children with admissions only, and the independent variables were defined by the year of the first admission. The number of admissions was counted for each child in the year of the first admission. As the number of admissions is a count variable with values greater than or equal to

1, truncated negative binomial regression was applied. DRG-weight of the first admission was used as a measure of cost and disease severity. DRG-weight was analysed with linear regression. DRG-weight was highly right-skewed and was therefore log-transformed. Also, the sum of DRG-weights in the first year with admission and sum of all DRG-weights throughout the period were calculated and included in the analyses.

To study whether the parental level of education could explain the geographic variation, we conducted sensitivity analyses, i.e., multilevel analysis with random intercept for the hospital referral areas. This was done for the survival analysis of admission and for DRG-weight. The analyses were stratified by gender and performed with restricted cubic splines (4 knots) for age. The full model with all the independent variables was compared with a reduced model without parental education.

3.3 Paper II - Cancer Care Pathways

3.3.1 Study population and data sources

A national registry-based study was conducted linking data from the Norwegian Patient Registry (NPR), the Cancer Registry of Norway (CRN) and Statistics Norway (SSB). The data included all Norwegian patients aged 18 years and above in CPPs for lung, colorectal, prostate or breast cancer (CPP patients) and patients diagnosed with lung, colorectal, prostate or breast cancer (cancer patients) in the period 1 January 2015 to 31 December 2017. Thus, two patient populations were analysed: i) CPP patients and the proportion without the relevant cancer and ii) cancer patients and the proportion included in the associated CPP.

3.3.2 Definitions and variables

Only the first CPP (NPR data) and the first cancer diagnosis (CRN data) for each patient were considered. The pathway type in the NPR data was matched on cancer diagnosis in the CRN data and vice versa. CPP patients without the associated cancer diagnoses were defined as CPP patients diagnosed without cancer.

Comorbidity was measured by a modified version of the Charlson comorbidity index (CCI) [103], based on diagnostic codes (ICD-10) from hospitalisations within one year prior to the start of the CPP or the cancer diagnosis, respectively. The index was categorised into low (CCI=0), medium (CCI=1) and high (CCI>1).

The travel time by road was calculated from the patients' municipality centre to the nearest hospital

and was categorised into short (less than 30 minutes), medium (30 to 60 minutes) and long (more than one hour).

3.3.3 Statistical analysis

The analyses for both CPP patients and cancer patients were stratified by gender and CPP type or cancer diagnosis. Separate analyses were conducted for i) patients in CPP and ii) patients with cancer diagnosis, for each of the six groups: lung (males and females), colorectal (males and females), prostate and breast (females only).

Two dichotomous outcomes were analysed by logistic regression; i) among CPP patients: the proportion diagnosed without cancer and ii) among cancer patients: the proportion included in the CPP. The following categorical independent variables were included in the statistical model: patients' age in age intervals, level of income and education, comorbidity, travel time and hospital referral area. Age interval 60 to 69 years, high level of education and income, low comorbidity, short travel time and Akershus hospital referral area (the largest one in terms of number of patients) were set as reference categories. Wald tests were used to assess the significance of the independent variables and potential interactions. P-values for linear trends over categories were calculated for four independent variables; education, income, comorbidity and travel time, by separate analyses with all the other independent variables included as categorical without any assumptions of a linear trend. For main effects, p-values <0.05 were considered statistically significant. Because of the large number of potential interactions involved, interactions were considered statistically significant if p-value <0.01. However, no statistically significant interactions were observed.

Age-adjusted proportions of CPP patients diagnosed without cancer and of cancer patients included in CPP, respectively, were calculated for the 21 hospital referral areas. The direct method of standardisation was applied. The reference populations were all CPP patients in the relevant CPP and all cancer patients with relevant cancer type, respectively, in the period. The Spearman's rank correlation coefficient was computed between the age-adjusted proportion of CPP patients diagnosed without cancer and the age-adjusted proportion of cancer patients included in CPP in patients living in different hospital referral areas.

3.4 Paper III - Atrial fibrillation and ablation

3.4.1 Study population and data sources

The study population was the complete cohort of all Norwegians aged 25 to 75 diagnosed with atrial fibrillation by Norwegian hospitals/specialist health care providers in Norway in the period 1 January 2008 to 31 December 2017.

3.4.2 Definitions and variables

The AF diagnoses were identified from the International Statistical Classification of Diseases and Related Health Problems (ICD-10) diagnosis code: I48 (primary or secondary diagnosis). The AF ablation procedures were identified from the Nomesco Classification of Surgical Procedures (NCSP) codes. Patients without an AF diagnosis prior to, or at the same date as, the AF ablation procedure were excluded.

Follow-up time was defined as the number of years from the first AF diagnosis to the event (ablation) or censoring (death, emigration, attained age 80 or 31 December 2017), whichever came first. Age, place of residence, income, and educational level were all defined according to the date of the first AF diagnosis. Patients with the date of censoring equal to the date of diagnosis were excluded.

3.4.3 Statistical analysis

Survival analysis was carried out separately for females and males by Cox regression with attained age as time scale. Age at the first AF diagnosis was treated as entry age to the study, regarded as left truncation time. AF ablation was considered as the relevant event, with education level, income level, place of residence and follow-up time since the first AF diagnosis as covariates. Follow-up time was time-dependent, while the other covariates were defined by the year of the first AF diagnosis. The categories representing high levels of education and income, Vestre Viken hospital referral area and South-East regional referral area and follow-up time within the first year were set as reference categories.

3.5 Data storage, approvals and ethical considerations

The studies are based on secondary use of clinical administrative data. For this reason, approval from Regional Committees for Medical and Health Research Ethics (REK) is not required, but REK has given exemption from the duty of confidentiality (ref. 20627/REK sør-øst A). The project has

conducted a Data Protection Impact Assessment (DPIA). This type of data are not publicly available. Access was given by applying to the NPR, the CRN and the SSB. According to Norwegian law, further ethical approval or obtaining informed consent was not required for this study. All methods were performed in accordance with the relevant guidelines and regulations.

Data from the Norwegian Patient Register (NPR), Statistics Norway (SSB) and the Cancer Registry of Norway (CRN) have been used in the publications. The interpretation and reporting of these data are the sole responsibility of the authors, and no endorsement by the NPR, SSB or CRN is intended nor should be inferred.

The original data were not collected by the authors, but made available by record-linkage, using the unique 11 digits personal ID, between NPR, CRN and SSB (NPR ref. 18/28584-13, CRN ref. 18/265 DU-3294 and SSB ref. W19/0477). Individual-level health data are, by definition, considered to be sensitive information in the Norwegian legislation, even if de-identified and strict confidentiality requirements prevent sharing of data in public repositories. According to a contract signed with the NPR, CRN and the SSB, the project is not allowed to forward data, or subsets of data, to other researchers, except project members named in the Data Protection Impact Assessment. Furthermore, we are required to delete the linked data set by 31 December 2023. However, any researcher with approval of an exemption from professional secrecy requirements for the use of personal health data in research from REK would be able to create an almost identical (updated) dataset by applying to the NPR, the CRN and the SSB.

4 Results

4.1 Paper I - Hospital admissions for children

A total of 1 538 189 children were included during 8 946 984 person-years. Of these, 156 087 children had at least one admission (10.2%). There were 198 293 admissions during the year of the first admission, with an average of 1.27 (standard deviation (SD) 1.12) admissions per child. The mean DRG-weight for the first admission was 0.76 (SD 0.59).

There was a near two-fold (1.9) difference in admission rates between the hospital referral areas (Vestfold HT: 3113 per 100 000 children, 95% confidence interval (CI) 3056 to 3169 vs OUS HT: 1627, 95% CI 1599 to 1654). There was a slight decrease in overall admission rates over time. Admission rates increased as the level of education for both the mother and father decreased. Children of mothers with low level of education had on average 36% higher admissions rates compared with children of mothers with high level of education (in 2016: 2587 per 100 000 children, 95% CI 2512 to 2662 vs 1810, 95% CI 1770 to 1849). This pattern was consistent for all hospital referral areas independent of total admission rates in each area.

The probability of admission increased with decreasing maternal and paternal level of education (low vs high maternal level of education (odds ratio (OR) 1.18, 95% CI 1.16 to 1.20), low vs high paternal level of education (OR 1.21, 95% CI 1.19 to 1.23)). The probability of admission decreased with increased maternal age (per five years: OR 0.94, 95% CI 0.93 to 0.94) and being an only child (OR 0.91, 95% CI 0.90 to 0.93). Results from multilevel analysis were similar. Multilevel analysis without parental level of education resulted in similar area level variance, indicating that differences in parental level of education do not explain the geographic variation and vice versa. Analysis stratified by child's age also found a negative parental educational gradient for almost all ages.

Children of parents with low or medium level of education had a higher number of admissions than children of parents with a high level of education (Incidence rate ratios (IRR) low vs high maternal level of education 1.05, 95% CI 1.01 to 1.10), low vs high paternal level of education (IRR 1.05, 95% CI 1.01 to 1.09)). The number of admissions per child increased with maternal age (per five years: IRR 1.03, 95% CI 1.02 to 1.05).

DRG-weight was highest for children of parents with high level of education. The differences from the reference category were less than 2%, but mostly statistically significant (low vs high maternal level of education (-0.5%, 95% CI -1.2% to 0.3%), low vs high paternal level of education (-1.9%,

95% CI -2.7% to -1.1%)). DRG-weight increased with maternal age (per five years: 1.2%, 95% CI 0.9% to 1.4%), while being an only child was associated with a lower DRG-weight (-1.1%, 95% CI -1.8% to -0.3%).

4.2 Paper II - Cancer Care Pathways

A total of 89 691 CPP patients and 49 787 cancer patients were eligible for analyses. Among all CPP patients considered, 56.9% ended up without the relevant cancer diagnosis. The proportion of CPP patients without the cancer diagnosis ranged from 43.9% for females in lung CPP to 69.3% for females in colorectal CPP. The proportion of CPP patients without the cancer diagnosis varied between the hospital referral areas, from 45.4% to 69.4% for all four CPPs combined. The variation in the proportions between the hospital referral areas was about two-fold across the CPP groups.

In total, 77.7% of the cancer patients were included in relevant CPPs, and the proportion increased from 72.0% in 2015 to 81.3% in 2017. The proportion of cancer patients included in CPP varied from 64.4% for prostate cancer to 92.7% for breast cancer, and between the hospital referral areas from 72.7% to 84.5% for all four types of cancer combined and more markedly across the cancer groups.

The adjusted analyses for all CPP patients showed an inverse age gradient, indicating lower odds of not receiving the cancer diagnosis with increasing age. An inverse age gradient was not consistently found in the adjusted analyses for the cancer patients.

A positive income gradient was found for male lung CPP patients, indicating increased odds of not receiving the cancer diagnosis with increasing income. However, for breast CPP patients the opposite was true. For the cancer patients, a positive income gradient was found, indicating increased odds of being included in CPP with increasing income, although the relationship was not statistically significant for female colorectal cancer patients.

A positive education gradient was found for patients for lung CPP (male and female) and prostate CPP, indicating increased odds of not receiving the cancer diagnosis with increasing level of education. For cancer patients no education gradient was found.

A positive comorbidity gradient was found for patients in colorectal CPP (male), prostate CPP and breast CPP, suggesting increased odds of not receiving the cancer diagnosis with increasing comorbidity. For cancer patients a clear negative comorbidity gradient was found for all cancer groups,

except breast cancer patients, i.e., decreased odds ratio of being included in CPP with increasing comorbidity.

No gradient for travel time was found for CPP patients. For cancer patients a positive gradient for travel time was found for patients with prostate cancer, the longer travel time to hospital, the higher the odds of being included in CPP.

Substantial differences were found between the hospital referral areas both regarding the odds of not receiving the cancer diagnosis among all the CPP patients and in the odds of being included in a CPP among cancer patients.

4.3 Paper III - Atrial fibrillation and ablation

In total, 23 159 ablation procedures were performed on 17 909 patients (all ages) in Norway in the period 2008-2017. The annual number of ablations increased in the period, with a marked increase of 65% from 2010 to 2011.

In the study population, a total of 88 534 patients aged 25-75 years were diagnosed with AF, 29 233 women (mean age at diagnosis 64.6 years) and 59 301 men (mean age at diagnosis 63.0 years). A total of 10 725 AF patients aged 25-75 years were treated with ablation in the period, 2 759 women (mean age at ablation 61.1 years) and 7 966 men (mean age at ablation 59.5 years).

A higher proportion of male AF patients were treated with ablation compared to female AF patients, and this was consistent in all age groups and follow-up years. However, the gender differences decreased with increasing age, and in the age groups 60-69 and 70-75 the differences were small.

The rate of ablation, in both female and male AF patients, increased with increasing levels of education. The effect of education was stronger in males than females. Patients with high level of education had around 60% and 35% higher rates of ablation in male and female patients, respectively, compared to patients with low education.

The rate of ablation in AF patients also increased with increasing levels of income. Similarly, as for level of education, the effect of income was stronger in males than females, with around 80% higher rate of ablation in male patients with high income and around 40% higher rate of ablation in female patients compared to patients with low income.

There was substantial variation within the RHAs. Patients living in the four hospital referral areas in

the North RHA all had lower rates of ablation, compared to patients living in the hospital referral area of Vestre Viken HT. Patients living in the hospital referral area of St. Olavs HT, in the Central RHA, had the highest rates of ablation in the country, and around three times higher ablation rates, than to patients living in the hospital referral area of Finnmark HT (3.9 fold higher for females and 2.9 fold higher for males).

The rate of ablation decreased with increasing number of years since AF diagnosis in both males and females in both models; however, the decreasing trend was not consistent throughout all the follow-up years.

It is important to note that the effects of education in both genders and the effects of place of residence in females differed over age groups. The strength of the positive relationship with educational level increased with increasing age.

4.3.1 Additional analysis - Paper III

In order to investigate whether the geographic variation could be explained by differences in SES, multilevel analysis with random intercept for the hospital referral areas or regional referral areas were conducted on the material in paper III. The gamma frailty model method for multilevel survival analysis as described by Austin was applied [104]. Table 1 shows the results of the full models and the reduced models with random intercept for referral areas. The reduced models are without education and income. The results from the multilevel analysis with the full models were similar to the results in the analysis in paper III. The multilevel analysis without education and income resulted in similar area-level variance as in the full models, indicating that differences in education and income do not explain the geographic variation.

A ordinary multivariable Cox regression model was also analysed (labelled as 'Ordinary' in Table 1), and the estimates for education and income from this model are similar to the estimates for education and income in the full multilevel model in Table 1. This also indicates that geography does not explain the socioeconomic variation. In addition, results from ecological analysis on proportions treated with ablation showed consistent positive education and income gradients across almost all the hospital referral areas for both males and females (Figure 2). This further strengthens the result from the multilevel analysis.

Table 1: Multilevel multivariable Cox regression models (with and without referral area) and ordinary multivariate Cox regression model, separate by gender. Random intercept for hospital referral areas (HT) and regional referral areas (RHA) in multilevel models. Variance is area-level variance. Hazard ratios (95% confidence interval), adjusted for follow-up time.

	Multilevel, full model (HT)		Multilevel, reduced model (HT)		Ordinary, full model (HT)	
	Female	Male	Female	Male	Female	Male
Education						
Low	1.0 (ref)	1.0 (ref)			1.0 (ref)	1.0 (ref)
Medium	1.31 (1.19 - 1.45)	1.28 (1.20 - 1.37)			1.31 (1.19 - 1.45)	1.28 (1.20 - 1.37)
High	1.34 (1.20 - 1.51)	1.63 (1.51 - 1.75)			1.34 (1.19 - 1.51)	1.62 (1.51 - 1.74)
Income						
Low	1.0 (ref)	1.0 (ref)			1.0 (ref)	1.0 (ref)
Medium	1.20 (1.10 - 1.31)	1.54 (1.42 - 1.67)			1.20 (1.10 - 1.31)	1.54 (1.42 - 1.67)
High	1.40 (1.23 - 1.59)	1.84 (1.70 - 2.00)			1.40 (1.23 - 1.59)	1.84 (1.69 - 2.00)
Follow-up time (years)						
1	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
2	0.68 (0.61 - 0.76)	0.86 (0.81 - 0.91)	0.68 (0.61 - 0.76)	0.85 (0.81 - 0.91)	0.68 (0.61 - 0.76)	0.86 (0.81 - 0.91)
3	0.63 (0.56 - 0.71)	0.64 (0.60 - 0.69)	0.63 (0.56 - 0.72)	0.64 (0.60 - 0.69)	0.63 (0.56 - 0.71)	0.64 (0.60 - 0.69)
4	0.58 (0.51 - 0.67)	0.70 (0.65 - 0.75)	0.58 (0.51 - 0.67)	0.70 (0.64 - 0.75)	0.58 (0.51 - 0.67)	0.70 (0.65 - 0.75)
5	0.68 (0.59 - 0.79)	0.62 (0.56 - 0.68)	0.68 (0.59 - 0.79)	0.61 (0.56 - 0.67)	0.68 (0.59 - 0.79)	0.62 (0.56 - 0.68)
6	0.73 (0.61 - 0.86)	0.63 (0.57 - 0.70)	0.73 (0.61 - 0.86)	0.63 (0.56 - 0.70)	0.73 (0.61 - 0.86)	0.63 (0.57 - 0.70)
7	0.85 (0.71 - 1.03)	0.63 (0.56 - 0.71)	0.85 (0.71 - 1.03)	0.62 (0.55 - 0.71)	0.85 (0.71 - 1.03)	0.63 (0.56 - 0.71)
8	0.63 (0.49 - 0.82)	0.62 (0.53 - 0.71)	0.63 (0.49 - 0.82)	0.61 (0.53 - 0.71)	0.63 (0.49 - 0.82)	0.62 (0.53 - 0.71)
9	0.62 (0.45 - 0.86)	0.59 (0.49 - 0.71)	0.63 (0.45 - 0.86)	0.59 (0.49 - 0.71)	0.62 (0.45 - 0.86)	0.59 (0.49 - 0.71)
10 or more	0.37 (0.21 - 0.66)	0.33 (0.24 - 0.46)	0.38 (0.21 - 0.67)	0.33 (0.24 - 0.46)	0.37 (0.21 - 0.66)	0.33 (0.24 - 0.46)
Random effect HT						
Variance	0.09858	0.05367	0.1008	0.06288		
	Multilevel, full model (RHA)		Multilevel, reduced model (RHA)		Ordinary, full model (RHA)	
Education						
Low	1.0 (ref)	1.0 (ref)			1.0 (ref)	1.0 (ref)
Medium	1.32 (1.19 - 1.45)	1.29 (1.21 - 1.38)			1.32 (1.19 - 1.45)	1.29 (1.21 - 1.38)
High	1.36 (1.21 - 1.53)	1.67 (1.55 - 1.79)			1.36 (1.21 - 1.53)	1.67 (1.55 - 1.79)
Income						
Low	1.0 (ref)	1.0 (ref)			1.0 (ref)	1.0 (ref)
Medium	1.20 (1.10 - 1.31)	1.54 (1.42 - 1.67)			1.20 (1.10 - 1.31)	1.54 (1.42 - 1.67)
High	1.37 (1.21 - 1.56)	1.82 (1.68 - 1.98)			1.37 (1.21 - 1.56)	1.82 (1.68 - 1.97)
Follow-up time (years)						
1	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
2	0.68 (0.61 - 0.75)	0.85 (0.80 - 0.91)	0.68 (0.61 - 0.76)	0.85 (0.80 - 0.91)	0.68 (0.61 - 0.75)	0.85 (0.80 - 0.91)
3	0.63 (0.56 - 0.71)	0.64 (0.59 - 0.69)	0.63 (0.56 - 0.71)	0.64 (0.59 - 0.69)	0.63 (0.56 - 0.71)	0.64 (0.59 - 0.69)
4	0.58 (0.50 - 0.66)	0.70 (0.64 - 0.75)	0.58 (0.51 - 0.67)	0.70 (0.64 - 0.75)	0.58 (0.50 - 0.66)	0.70 (0.64 - 0.75)
5	0.68 (0.58 - 0.79)	0.62 (0.56 - 0.67)	0.68 (0.59 - 0.79)	0.61 (0.56 - 0.67)	0.68 (0.58 - 0.79)	0.62 (0.56 - 0.67)
6	0.73 (0.61 - 0.87)	0.63 (0.57 - 0.70)	0.73 (0.61 - 0.87)	0.63 (0.56 - 0.70)	0.73 (0.61 - 0.87)	0.63 (0.57 - 0.70)
7	0.86 (0.71 - 1.03)	0.63 (0.56 - 0.71)	0.85 (0.71 - 1.03)	0.63 (0.55 - 0.71)	0.86 (0.71 - 1.03)	0.63 (0.56 - 0.71)
8	0.64 (0.49 - 0.82)	0.62 (0.53 - 0.72)	0.64 (0.49 - 0.82)	0.62 (0.53 - 0.71)	0.64 (0.49 - 0.82)	0.62 (0.53 - 0.72)
9	0.63 (0.45 - 0.86)	0.59 (0.49 - 0.71)	0.63 (0.46 - 0.87)	0.59 (0.49 - 0.71)	0.63 (0.45 - 0.86)	0.59 (0.49 - 0.71)
10 or more	0.37 (0.21 - 0.66)	0.33 (0.24 - 0.46)	0.38 (0.21 - 0.67)	0.34 (0.24 - 0.47)	0.37 (0.21 - 0.66)	0.33 (0.24 - 0.46)
Random effect RHA						
Variance	0.09244	0.05040	0.09328	0.05475		

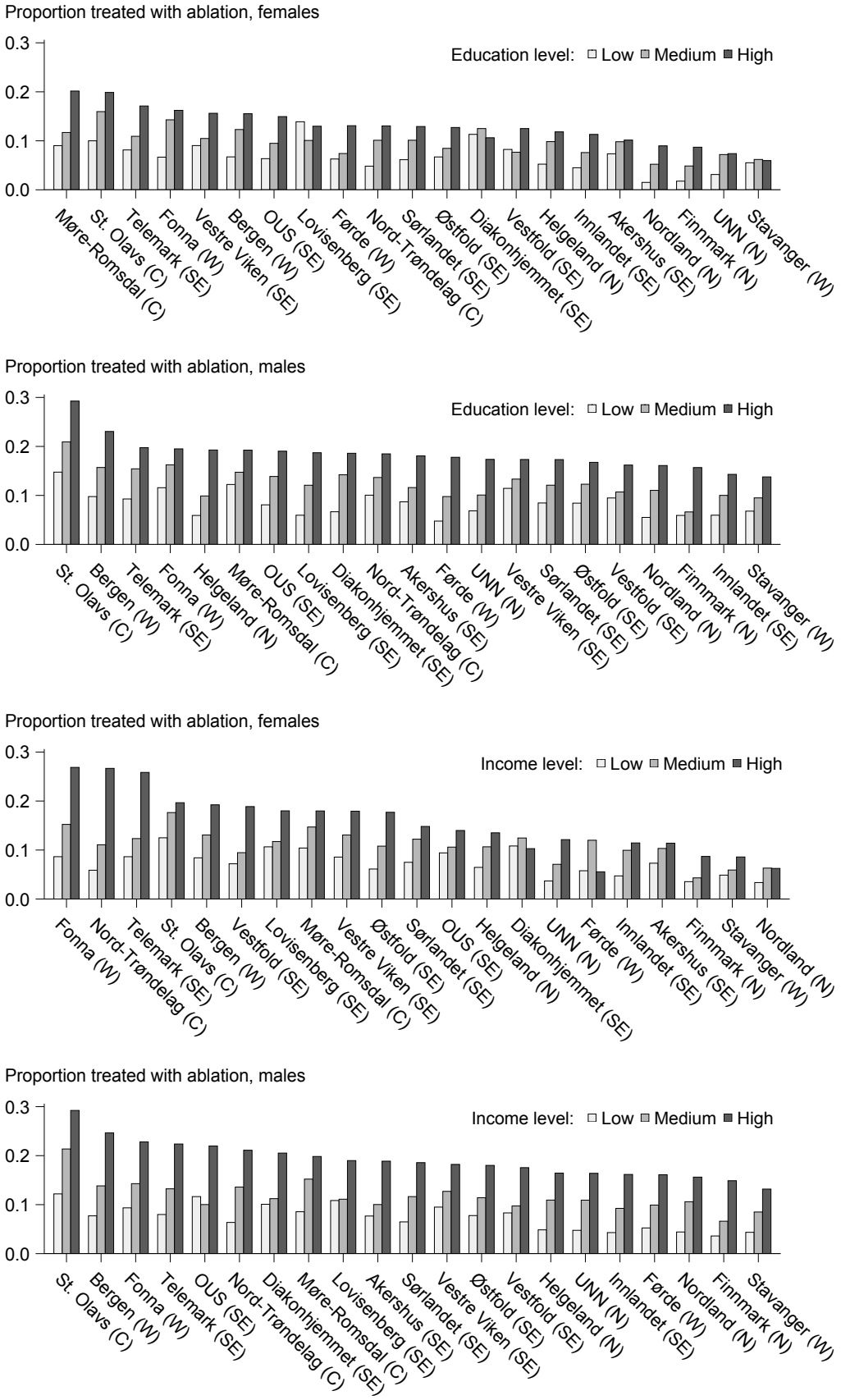

Figure 2: Proportions treated with ablation by hospital referral areas, stratified by gender, education and income level.

5 Discussion

The overall aim of this thesis was to generate more knowledge about and explanations of variation in the utilisation of health care services in Norway. This has been done by exploring geographic and socioeconomic variation in the use of three different health care services in Norway. In addition, the aim was to investigate whether geographic variation could be explained by differences in socioeconomic status. The results from our research contribute to the field of health services research and question the equality in access to health care in a universal health care system. However, there are also limitations. In this section, some methodological considerations are first presented before the discussion of main results.

5.1 Methodological considerations

Health service research studies how social factors, financing systems, organisational structures and processes, health technologies, and personal behaviours affect access to health care and the quality and cost of health care [105]. Health services research is a multidisciplinary field of epidemiological, sociological, economic, and other analytic sciences in the study of health services. Health services research covers several fields, including studies of the phenomenon of practice variation [106]. The papers in this thesis are examples of health services research applying epidemiological methods.

5.1.1 Study design

Epidemiological studies aim to contribute to understanding the frequency, pattern, and causes of disease or health-related events [107]. The papers in this thesis apply epidemiological methods to study associations between multiple exposures and outcomes. Analytical epidemiological designs can be divided into two categories; experimental or observational design [108]. In studies with experimental designs, the exposures (the intervention) are determined by the investigator, and normally allocated at random to avoid confounding. Observational studies are studies that observe without intervening and make use of variation in exposure that occurs in populations. Ecological observational studies are studies where populations or communities are the unit of analysis. In this thesis, the individual is the unit of analysis. There are three categories of observational studies on individuals; i) Cross-sectional - studies of a defined population (or a random sample thereof) at a fixed point or period of time, ii) Case-control - retrospective studies with groups classified by the outcome (disease/not disease), iii) Cohort - studies of a population over a defined time-period to assess the proportion that develops the outcome/disease of interest. Cohort studies can be retrospective or prospective. In retrospective

cohort studies, the exposure and outcomes have already happened. They are usually conducted on data that already exists and the exposures are defined before looking at the existing outcome data to see whether exposure to a risk factor is associated with a statistically significant difference in the outcome development rate. If there is a temporal sequence between exposure and outcome, it is appropriate to define the study as a study with a historical prospective cohort design [109].

The papers (I-III) in this thesis may all be considered observational studies with a historical prospective cohort design. In 2018, historical data were extracted from various sources for three different time periods; 2008-2016 in paper I, 2015-2017 in paper II, and 2008-2017 in paper III. Thus, data were collected retrospectively, and the exposure came before the outcome. For the second population in Paper II (the cancer patients), it is not a prospective study, as inclusion in CPPs comes before cancer diagnosis in time, and it is more correct to classify this as a cross-sectional study of cancer patients. In epidemiology, the term exposure can be applied to factors that may be associated with an outcome of interest, and these can also be referred to as risk factors. In the papers, we have studied the associations between multiple exposures/risk factors and outcomes, and we have mainly used the term exposure variables or simply covariates.

5.1.2 Bias, interaction and confounding

All epidemiological studies are potentially susceptible to errors, and the types of errors are typically divided into random error and systematic error. Errors may arise because of the study design, the conduct of the study, the analysis of the study, and the interpretations in the study. Random error typically affects comparison groups equally and reflects a problem of precision. The impact of random error can be reduced by increasing the sample size. Systematic error affects comparison groups unequally and is due to selection bias and information bias. Selection bias occurs when the study sample is not representative of the population of interest, and information bias involves misclassification or measurement error of exposure or outcome. When planning an epidemiological study, handling variable selection and statistical modelling is important in order to avoid biased results. Confounded and modified effects (effects modification/interaction) are two situations that need to be considered. Confounding refers to a situation where a non-causal association between an exposure and an outcome is observed because both exposure and outcome are related to one or several other variables causing the association [110]. Statistical interaction occurs when the effect of a risk factor on the outcome is modified by the value of another independent variable in the analysis [111]. The major weakness of observational studies is bias and confounding.

Selection bias

The term selection bias refers to ”when a systematic error in the recruitment or retention of study participants (...) results in a tendency toward distorting the measure expressing the association between exposure and outcome” [111].

Selection bias occurs when the association between exposure and outcome estimated for those who participate in the study is different from the association that would have been found if the whole study population participated [112]. The studies in this thesis define the patients from contacts with the publicly financed health services. In all the three papers, complete Norwegian populations are studied, thus selection bias is for all practical purposes eliminated. In paper I, the complete national population cohort of children, both admitted and non-admitted, and their parents were studied. In paper II, the complete national populations of CPP patients and cancer patients (for four selected CPPs and cancer types) were studied. In paper III, the complete national population of atrial fibrillation patients was studied. Privately financed health services are not included, as there are no available data on privately financed health services in Norway. This might lead to selection bias as the better-off probably use private health care to a greater degree than the worse-off. However, compared to other countries there is a limited private out-of-pocket or insurance-based health service supply in Norway, and with some minor reservations discussed below, virtually all patients are included in the studies.

In paper II, it was not possible to evaluate at which point in the diagnostic and staging work-up patients are included in CPPs, making possible the retrospective inclusion of cancer patients into CPPs. Unclear guidelines lead to some degree of retrospective inclusion in the first implementation period of the first CPPs, and the practice probably varied between hospitals. In addition, some patients without cancer have been evaluated for cancer without having been included in CPPs. This could cause bias, however this probably only applies in the first part of the study period and for a very small proportion of the patients. In paper III, patients treated with ablation without a prior AF diagnosis were excluded. Some patients have been diagnosed in primary health care and some patients have been diagnosed with AF prior to the study period. However, all patients eligible for ablation should have been diagnosed by specialist health care services. Differences in waiting times for ablation might lead to selection bias, as the number of ablation patients diagnosed prior to the study period then would differ between the ablation centres. However, the overall waiting time has been about the same in all the ablation centres in the period, while we have no information about waiting times according to age, gender, and SES. Different waiting times between SES groups could cause selection bias.

Information bias

Information bias or misclassification bias are terms used to describe systematic errors that occur in a study when the value of exposure, outcome and/or covariates used in the analysis are systematically different from the true value of these variables, due to measurement errors in continuous variables or misclassification of categorical variables [113]. In this thesis, the status of exposures and outcome is based on information from different linked registers. One possible pitfall is that the information in the registers is collected for other purposes than the aim of this thesis.

In prospective cohort studies, information bias is a more frequent problem than selection bias and is important to consider. The data used are from national and public registers and have good quality and high completeness. Even though the data used in this thesis have good quality, misclassification might be an issue, and more so for diagnosis codes, than procedure codes. All Norwegian hospitals must submit data to the Norwegian Patient Registry (NPR) for registration and reimbursement purposes, and all Norwegian cancer cases are to be reported to CRN. The selected NPR and CRN variables have good data quality and high completeness [114–116]. Recall bias from self-reporting was avoided by using register data. Misclassification in administrative data is a possible source of error in the papers in the thesis, as the study populations are defined by diagnosis and/or procedure codes. In paper I, where hospital admission is the main outcome there is no reason to suspect misclassification to any extent. Bias may occur due to changes in exposure during the period, however, we have yearly data on income, education and place of residence, and income was also index-adjusted by the consumer price index (CPI) to account for inflation. In paper II, CPPs were studied in the period 2015-2017. CPPs in Norway were implemented in 2015, and there might have been problems related to IT systems, registration practice and uncertainty about the system in the start-up period causing misclassifications [117]. In paper III, there might be an issue with the diagnosis of atrial fibrillation. The ICD-10 code I48, primary or secondary diagnosis, was used to define the AF patients. Coding errors are not unusual, and especially secondary diagnosis codes can be prone to misclassifications. In addition, the ICD-10 code I48 for atrial fibrillation was used to identify the patient population in this study. This also includes atrial flutter. Until 2013 it was not possible to distinguish, by ICD-10 codes, between atrial fibrillation and atrial flutter, as the third digit in the I48 code first was introduced in 2013. Atrial fibrillation is a much more common condition than atrial flutter, but still this means that the actual number of atrial fibrillation patients is somewhat lower than reported. However, the separate analysis for the period 2013-2017, with atrial fibrillation patients only (ICD-10 codes: I48.0, I48.1, and I48.2), showed similar associations as the main analysis for the period 2008-2017.

Using historical data, some of the time and cost disadvantages of cohort studies were overcome, and we avoided information biases usually associated with case-control design. However, a retrospective cohort design also implies some methodological limitations. Relying on registry data, we study data registered for other purposes, and without the possibility of influencing what information was collected. The data collection process is not under the control of the researchers, nor are possible changes in the collection procedures over time.

Effect modification and interaction

Statistical interaction occurs when the effect of an exposure variable or a risk factor on the outcome is modified by the value of another independent variable in the analysis [118]. Dealing with interactions can be done by stratifying the analysis or by including interaction terms in the statistical models.

In the three papers, different types of multiple regression methods have been applied, with mutual adjustment for the selected covariates. In paper I, due to high correlation between parents' age, only mother's age was included in the analysis. Because of interaction between age and gender, restricted cubic splines for age with interaction term for gender were applied. In addition, analyses stratified by children's age were also conducted, and an inverse parental education gradient was found for almost all ages. In paper II, the analysis was stratified by gender. In paper III, the analysis was stratified by gender, and because of interactions between attained age and education in both males and females and place of residence in females, the analyses were also stratified by age groups.

Covariate selection and confounding

In observational studies, covariate selection, i.e., adjusting for potential confounders and avoiding over-adjustment is a major concern [110]. Confounding can be controlled or adjusted for in several ways, by restriction, matching, stratification or multivariate adjustment techniques [113].

In regression methods, as used in all three papers, confounding has often been identified through statistical associations, using e.g., stepwise selection methods. However, such methods are not based on a priori understanding of the causal relationship between the variables under study [112]. Directed acyclic graphs (DAG), also called causal diagrams, are graphical representations of the causal relationships believed to exist between the variables of interest [119]. As a cause must precede its effects, the graphs are always acyclic. DAGs help to identify confounders, mediators and colliders. Confounders are common causes, mediators are transmitters and colliders are common consequences. Confounders should always be adjusted for in order to remove bias. The confounder can be included as a covariate in the regression, or the analysis can be stratified by the confounder. Mediators should be

adjusted for to analyse the direct effect of the exposure variable on the outcome. However, in order to study the total effect of the exposure on the outcome one should not adjust for the mediator. Colliders should never be adjusted for, as adjustment will lead to bias.

In paper III, we found that the effect of education on ablation probability increased with age. Independent of age, healthy patients are stronger candidates for ablation. The SES gradient in health is well documented [120]. A Swedish study found that the gradient increased with age, i.e., lower SES groups had faster health deterioration over time than higher SES groups [121]. The association between SES, age and ablation probability might partly be explained, i.e., be confounded, by the increasing differences in health between SES groups with increasing age. The simplest method to adjust for confounding is stratification, as we did for age and gender in Table 3 and 4 in paper III.

In all the three papers, multivariable regression models were applied, as we were interested in several exposure variables associated with the outcomes. This is a somewhat different setting than in some other epidemiological studies with one main exposure adjusted for confounding and interaction. In paper II, the analysis was stratified by gender, and the selection of the independent variables, i.e., adjusting for potential confounders, was assessed in separate analyses by causal diagrams or the DAG methodology [122]. In the DAG in Figure 3 the variables in paper II are linked by arrows that represent direct causal effects of one variable on another variable. The outcome is either i) CPP patients; the probability of being without the cancer diagnosis or ii) Cancer patients; the probability of being included in a CPP. Often causal pathways are not fully understood, this is also the case in this thesis, and the assumptions about the arrows in the DAG in Figure 3 can be debated.

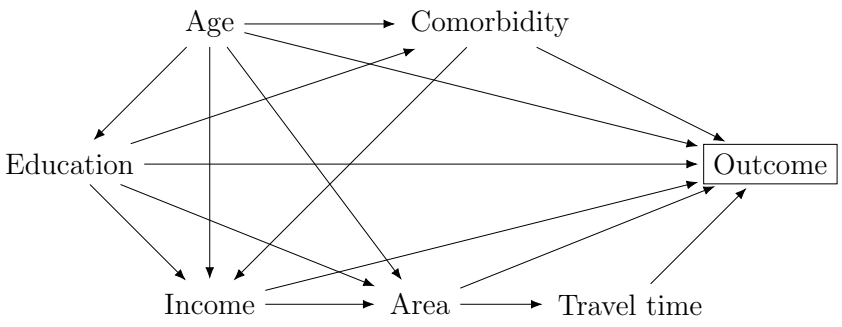

Figure 3: Directed Acyclic Graph of variables in paper II

5.1.3 Causality

A principal aim of epidemiology is to understand the causes of disease variation [107]. In observational studies the study groups are not determined by randomisation. Randomised experiments usually have

advantages compared to observational studies for making casual inference, since it is not possible to control for all possible variables in observational studies [123]. In addition, many variables are difficult to measure. Therefore, in observational studies, a number of possible explanations for an observed association, as discussed above, need to be considered before we can infer that a cause-effect relationship exists.

When considering the relationship between exposures and outcomes, it is important to distinguish between association and causation. Epidemiologists ultimately want to conclude about causation, but most epidemiological studies focus on establishing associations. In order to assess whether such associations are causal all epidemiological noise (random effects, bias and confounding) should be eliminated. In general, this is only possible to achieve in clinical trials, and due to both practical and ethical considerations causality cannot, in general, be proved in observational studies [124]. The studies in this thesis are not able to demonstrate the causes of variation and focus on associations, rather than causality.

5.1.4 Validity and generalisability

Generalisability of the results in epidemiological studies is related to external validity. External validity is conditional of internal validity, i.e., the results are not externally valid if they are not internally valid. Internal validity refers to how accurately the results represent the relationships in the source population, i.e., are the results of the study true, or are they an artefact of the way the study was designed or conducted [125]. Bias and confounding are related to internal validity. External validity refers to the generalisability of the study to other populations than the study population, i.e., are the study results likely to apply, generally or specifically, in other study settings or samples [125]. All three papers in this thesis give results from entire Norwegian populations (in particular age groups). Thus, we are studying complete populations, and statistical inference is commonly said to be inapplicable to complete population studies [126]. However, studies of complete populations have become more common, and they often report p-values and confidence intervals. The use of statistical inference implicitly requires a target population that is wider than the complete population under study [126]. Examples of target populations can be future cases or a geographic region greater than the region under study. The validity of the statistical analysis then depends on the generalisability of the complete population to the target population. The findings in this thesis are assumed to be representative in similar types of health care services in countries or regions with universal health care services.

5.2 Discussion of main results

In this section, the results from the three articles are seen in context, and the overall findings and possible explanations are discussed. The results are discussed in detail in the three papers.

5.2.1 Geographic variation

Substantial geographic variation in health care use was found in all three papers. The variation between referral areas, measured as the highest rate divided by the lowest rate, i.e., the extremal quotient (EQ), was about two-fold in medical hospital admissions for children in paper I. In paper II, a two-fold variation was also found in the proportion of CPP patients without the cancer diagnosis, while the proportion of cancer patients included in CPP the EQ was around 1.3. In paper III, the variation in the proportion of AF patients treated with ablation therapy between the hospital referral areas was three-fold.

It is not reasonable to categorised the three studied health care services as effective care according to the Wennberg terminology [51]. It is probably more correct to categorise the three health care services as combinations of preference-sensitive and supply-sensitive care. Then, according to both Wennberg and Sutherland, if the observed geographic variation is not due to differences in disease prevalence or patient preferences between the hospital referral areas, it is unwarranted [12, 53].

There is no systematic monitoring of geographic differences in health or disease prevalence in Norway. A study on geographic health inequalities in Norway found relatively low levels of geographic inequalities and the absolute inequality in mortality and life expectancy between Norwegian counties (almost similar to hospital referral areas) decreased from 1980 to 2014 [127]. Even though the inequalities are low there are still differences, and Finnmark is the county with the highest mortality and the slowest decrease in mortality rate [127]. Finnmark, and Northern Norway, has also historically had the highest cardiovascular mortality, while cardiovascular mortality has been lowest in Western Norway. However, also the differences in cardiovascular mortality have been substantially reduced the past decades [128]. Also for cancer, there are known geographic differences in incidence and mortality in Norway [129]. Differences in disease prevalence is a matter of concern mostly in paper I. In paper I we compared the number of children admitted to hospital between geographic areas. The population was all Norwegian children. Differences in disease prevalence between these areas, without adjusting for it, would lead to biased results. In contrast, in paper II and III the populations are patients (in paper II: CCP patients and cancer patients and in paper III: AF patients) and we compared the proportions

of these patients on their different outcomes. Therefore, differences in disease prevalence between the areas would influence the size of the study populations in the areas, but it would not cause biased results. There is a lack of knowledge about geographic variation in disease prevalence in children in Norway. A study on asthma, hay fever and eczema showed small geographic differences in incidence [130]. However, this study did not cover the entire country. Two studies on self-reported asthma found similar prevalence in the county of Nordland and Oslo [131, 132].

The concept of informed patients and patient preferences are important aspects in the definition of unwarranted variation by both Wennberg and Sutherland. However, the terms informed patients and patient preferences lack a consistent definition. Unless the patient actually is the medical expert on the field, the patient can probably never be fully informed. A review study on patient comprehension of informed consent found that comprehension, in general, was low [133]. However, a Cochrane review shows that patients exposed to decision aids feel more knowledgeable, better informed, and they probably have a more active role in decision making and more accurate risk perceptions [134]. In the review, no adverse effects on health outcomes or satisfaction of decision aids were found, and treatment rates were either decreased or no different when comparing patients with and without decision aids [134]. Wenneberg, therefore, claims that patient decision aids can improve the quality of clinical decision making, and hence treatment decisions are more in line with the patient's underlying preferences [51]. In order to measure patient preferences and the impact on geographic variation, survey data has been applied in several studies [49, 135, 136]. Cutler et al. used survey questions to physicians and patients to differentiate between patient demand-side factors and physician supply-side factors of geographic variation [49]. They measured patient preferences by asking about a variety of aggressive and/or palliative care interventions, and they conclude that patient preferences are not important in explaining variations. A similar result was found by Baker et al., by measuring preferences from six survey questions together with supply-side data on area level [136]. Anthony et al. also found that patients' preferences for seeking primary and specialist health care did not play a significant role in explaining geographic variation in health care use [135]. We are not aware of similar studies of patient preferences in Norway, but it is reasonable to assume that the effect of patient preferences on geographic variation is small also in Norway.

Based on the knowledge about disease prevalence and patient preferences, we assume that differences in disease prevalence and patient preferences between the hospital referral areas cannot justify the differences in utilisation. Therefore, the observed geographic variation in these studies is characterised as unwarranted. Cancer patients included in CPP in paper II might be an exception. However, the

outcome measure is the proportion of cancer patients included in CPPs, and the baseline proportions are high for all cancer groups. EQ measures will therefore be smaller for any given difference between hospital referral areas as compared to smaller baseline proportions.

In paper I, the analyses based on individual data supported the results from the ecological analyses of admission rates. Geographic variation in health care utilisation for children has been described both in publicly financed and privately financed health care systems [69, 71, 72]. The Norwegian Child Healthcare Atlas [69] and the Neonatal Healthcare Atlas [73] found relatively large geographic variation between hospital referral areas in admission rates and rates of treatment procedures over a period of five years. Our present study confirmed these findings over a period of 9 years.

It is reasonable to assume that the observed variation between the hospital referral areas is related to both differences in clinical practice and differences in capacity. The same is concluded in a recent review article on unwarranted geographic variation in paediatric health care in the United States and Norway [137]. Although utilisation of health care resources sometimes is interpreted as an indicator of prevalence, this is hardly correct taking into consideration the large geographic variation found by us and others [69, 71, 72]. In an internal benchmarking of Norwegian paediatric departments in 2013, the number of staffed beds in paediatric departments, as reported by the departments, varied between 41 and 107 beds per 100,000 children [69]. There was a positive association between the admission rates reported in the Norwegian Child Healthcare Atlas and the number of staffed beds in the hospital referral areas [69].

In paper II, substantial variation between the hospital referral areas was found, both for the proportion of CPP patients without the cancer diagnosis and the proportion of cancer patients included in CPP. The proportions in neighbouring hospital referral areas were not more similar than for more distant hospital referral areas. It was not consistently the same hospital referral areas that had the highest or lowest proportions of CPP patients without the cancer diagnosis or the highest or lowest proportions of cancer patients included in CPP.

Differences in the number of out-patient clinics and diagnostic work-ups capacity between the hospital trusts may cause variation. In the study period, e.g., prostate cancer diagnostics was only performed at one hospital (UNN Tromsø) in the North RHA. Since the diagnostic work-ups for the different CPPs are done at different departments/units in the hospitals, it is reasonable to see varying degrees of inclusion to CPP in the hospital referral areas across the different CPPs. A hospital might have a lower threshold for including patients in CPP in some areas due to capacity or clinical practice while

having a higher threshold for other areas due to capacity constraints or stricter clinical practice. In addition, some hospital trusts have public funding contracts with private specialists in order to secure sufficient capacity, e.g., in mammography and coloscopy. Different utilisation of private specialists among the hospital trusts may also contribute to the observed variation. Additionally, hospitals may have included patients in CPPs at somewhat different points in the diagnostic and staging process, although clear guidelines exist. This may also explain parts of the observed variation.

In paper III, substantial geographic variation was found in the probability of ablation according to the patients' place of residence, both considering hospital referral areas (HT) and regional referral areas (RHA). Geographic variation in ablation utilisation has been documented in studies from both Europe and the US [138, 139]. Also, among Medicare beneficiaries in the US marked geographic variation in the use of catheter ablation for atrial fibrillation was found, and it was not associated with the prevalence of atrial fibrillation, availability of cardiologists or end-of-life resource use [140].

The reasons for the observed variation in the ablation rate are not clear, but may reflect provider preferences and uncertainty of safety and/or efficacy of the procedure in a region. Differences in ablation capacity at the five ablation centres may also contribute to the observed geographic variation. The ablation procedure in Norway was first implemented in 2001 at Haukeland University hospital in Bergen HT (West RHA), in 2004 at Rikshospitalet in OUS HT (South-East RHA), in 2005 at St. Olavs hospital in St. Olavs HT (Central RHA), and in 2009 at UNN Tromsø hospital in UNN HT (North RHA). Ablation treatment was lastly implemented in the North RHA, and in the study period only one physician has been performing the procedure at UNN Tromsø Hospital. Although data on ablation capacity is lacking, we can with some certainty assume that the North RHA has had the lowest per capita capacity, and the proportions treated with ablation were in general lowest in the hospital referral areas in the North RHA. Almost all ablation patients living in the referral areas of West (98%) and Central RHA (97%) were treated at their respectively ablation centres, while only 63% of ablations patients living in the referral area of North RHA were treated at UNN Tromsø hospital (9% at St. Olavs (Central RHA), 23% at Haukeland (West RHA), 4% at Rikshospitalet (South-East RHA) and 11% at the private subcontractor). Ablation patients living in the South-East RHA were treated at Rikshospitalet (74%) and at the private subcontractor (23%). The ablation centre UNN Tromsø hospital (North RHA) serves the population in Northern Norway, i.e., around 9% of the Norwegian population. In the period 2008-2017 only 5% of the ablations in Norway were performed at UNN Tromsø Hospital, this is partly due to the late implementation of the procedure and partly due to restricted capacity.

Substantial geographic variation was found in all three papers, and we have characterised it as unwarranted as the variation most probably is related to differences in clinical practice and capacity, and probably to a lesser extent related to differences in patient preferences and medical needs between the hospital referral areas.

5.2.2 Socioeconomic variation

Socioeconomic variation was found in all three papers. However, in paper II, we only found this consistent for the cancer patients, i.e., an inverse association with income. In paper I, SES was measured by parental education level, while in paper II and III SES was measured by both income and education level. In both paper I and III the socioeconomic variation was consistent in all the hospital referral areas.

In paper I, children of parents with low level of education had the highest admission rates, while children of parents with high level of education had the lowest admission rates. This was consistent both over time and across hospital referral areas. The inverse gradient between admission rates and parents' level of education is in accordance with findings by others [35, 141, 142]. Similar results have also been found for adults in systems with universal health care coverage [143]. We also found an inverse association between the number of admissions per child and parental education level. However, the association between the level of parental education and DRG-weight was positive, suggesting that the conditions causing the admission were slightly less severe among children with lower SES. Previous studies have found higher treatment costs for children with low SES [34, 35, 144]. The contrast with previous studies may be related to measurement of SES. We used individualised paired data for each child-parent couple at the year of admission, while most other studies apply ecological SES measures.

In paper II, the effects of income and education were not consistent across the CPP groups. In a report on social inequalities and cancer incidence in Norway [145], associations between both income and education level and the cancer incidence were found. The incidence of cancer increased with low level of income for males for lung and colorectal cancer, and increased incidence of cancer with low level of education was found for lung cancer and among females for colorectal cancer. In contrast, increased incidence of cancer with high levels of income and education was found for prostate and breast cancer. The observed differences in the odds ratio of not receiving the cancer diagnosis between the income groups for CPPs for lung (male) and breast cancer, in paper II, might be due to different risks of cancer in the income groups between the CPPs.

The probability of being referred to a CPP, both for those with and without cancer, may also differ between income and education groups. Based on data in this study, only the probability for those with cancer can be estimated (see Appendix A in paper II). The observed differences in income and education gradients for CPP patients without the cancer diagnosis may diminish when the risk of cancer and the probabilities of being included in a CPP are taken into consideration.

The proportion of cancer patients included in CPPs was highest in the patients with high income, which is in line with a recent Norwegian study [117]. However, in accordance with results of Nilssen et al. [117], we found no such effect of education for any of the cancer groups.

In paper III, we found that AF patients with a high level of education and a high level of income were more frequently treated with ablation. These inequalities increased with increasing age. However, no statistically significant effect of education was found in the youngest females.

For coronary heart disease, socioeconomic differences in revascularisation procedures have been reported in several European countries [146–149]. A systematic review of associations between socioeconomic status, atrial fibrillation, and outcomes found no consistent social gradient in the risk of AF [150]. However, if AF was present, there was a social gradient in the risk of poorer outcome. Low SES was associated with poorer treatment, less knowledge, poorer psychological health and higher mortality. A nationwide Danish study found small differences between SES groups in the risk of being diagnosed with AF, although for the younger higher SES was associated with lower risk of being diagnosed with AF [151]. In another study from Denmark, socioeconomic differences were documented in outcomes after hospital admission for atrial fibrillation or flutter, both in mortality and treatment with ablation [152]. A Norwegian study indicated that low SES was related to higher mortality in AF patients [153].

The results in the three papers in the present thesis are mostly in line with other studies, however, most other studies apply ecological measures of SES. One major strength of the papers in this thesis is the use of individual data also on SES, and we are thereby also avoiding the problems associated with ecological fallacy.

5.2.3 Social inequality in health care utilisation

Socioeconomic differences in use of health care services have been discussed extensively, also in countries as Norway with universal health care systems, where there is no co-payment from the patients for in-hospital treatment.

Studies have shown that low SES is associated with higher use of GPs [47], while the use of health care specialists is associated with higher SES [4]. Even when adjusted for health needs, those with higher SES are still more likely to use specialist health care [154]. The positive association between utilisation of specialist health care and SES may be seen as a public health paradox, since there is generally more need for health care among lower SES groups.

Out-of-pocket payment or lack of health insurance may be an obstacle to disadvantaged groups seeking health care [45]. All health care for children under the age of 16 in Norway is free of charge, and parents are economically compensated for the loss of income if admitted to hospital with their child. Privately financed ablations are not included in paper III, as data on privately financed procedures were not available. However, close to all ablation procedures in Norway are financed by the public health service, and the same goes for cancer treatment. This most likely excludes a significant effect of economic restraints on access to specialised health care.

Thus, there must be other factors explaining the variation associated with SES. There may be significant differences in disease prevalence and medical needs or informed preferences related to patients' or parents' level of SES.

There is increasing evidence of the positive relationship between SES and health outcomes throughout the lifespan [155]. However, most SES factors influencing health status are related to exposure over time, during a critical period or through the pathway of learned lifestyle. As a consequence, the major impact of SES on health becomes apparent during the second half of a normal lifespan, not during childhood [156].

Despite the social gradient in health also for children, the disease prevalence in children is not consistently higher in those with low SES for all diseases. The majority (55%) of the admissions included in the analyses in Paper I are related to allergies, eczema, respiratory tract infections, and gastrointestinal infections. The association between SES and the prevalence of asthma, allergies and atopic disease in children is disputed. In a study on children with chronic health conditions in the Nordic countries in 1996, the prevalence for all the diagnostic categories was higher among children from low education worker, or low-income families [157]. However, according to several studies atopic disease, allergies, and nervous system tumours occur more frequently among children with high SES [158–161]. A German cross-sectional study concluded that only a few health indicators such as obesity occurred more frequently in socially disadvantaged children [160]. Evidence from a systematic review suggests that there is a negative social gradient in the prevalence of asthma, and

a positive social gradient in the prevalence of allergies [162]. A Danish study found that atopic eczema in children was associated with high parental educational level, whereas asthma and hay fever were associated with low parental education level [163]. A study on socioeconomic risk factors for bacterial gastrointestinal infections found that risk of infection was associated with increasing socioeconomic status [164]. Although we acknowledge that there is a social gradient in disease prevalence in Norwegian children, it can be questioned whether the differences in disease prevalence between the education groups are the main cause of the variation in admission rates between education groups for Norwegian children found in paper I.

Parents in higher SES groups might have more knowledge about medical issues and conditions, and might therefore be able to take more preventive steps to ensure that their children avoid hospital admission. A study on avoidable paediatric hospitalisations found that children from poor families are at greater risk for avoidable hospitalisations [165]. Better knowledge about the child's medical condition and avoiding known disease triggers might reduce the number of avoidable admissions [165].

Individuals assess their health differently, and highly educated people are reported to assess their health more negatively than their less educated counterparts [6]. Variation in health expectations, as reflected by health assessment, might be one of the drivers of inequality of health care utilisation across SES groups. There are several explanations to this variation in assessment of health by education. The conceptions of good health and the health expectations are contingent on the knowledge of disease and available treatments [166]. Highly educated individuals have superior information acquisition skills and are thereby more prone to recognise and report symptoms of disease [6]. Individuals also assess health relative to the average level observed among their respective peers, and due to the negative education gradient in health this may generate peer effects [6]. The socioeconomic gradient in physical activity is also well known. Individuals in higher SES groups are more physically active compared to individuals in lower SES groups [167]. Thus, individuals in higher SES groups might be more affected by health issues and symptoms of disease might be revealed at an earlier stage. In addition, higher SES groups might also be more eager to be included in CPPs in order to assess their cancer symptoms. It is documented that individuals with lower SES are less likely to participate in cancer screening programs [168, 169]. A systematic review concluded that women in Europe from more socioeconomically deprived areas were less likely to attend breast cancer screening [169]. in contrast, in Paper II we found no SES gradient in CPP patients without the diagnosis, and one interpretation might be that CPP as a health service in Norway is equitably distributed.

Alternatively, the variation associated with SES may be related to other factors than the patient's health status or the patient's perceived health status. Studies have shown that patients' socioeconomic status is associated with an increased likelihood of access to cancer care [170, 171]. Our finding, that patients with higher SES are over-represented among those who undergo ablation therapy and cancer patients included in CPPs, is in accordance with several other reports of such gradients in the use of specialised health care, both international and from Norway [3, 4, 172]. This might indicate that manoeuvrability related to higher education and social capital increases the chances of treatment in a specialised hospital. It is documented that patients from higher social classes communicate more actively with clinicians [173].

Health literate patients or parents may be more capable of understanding, questioning and discussing treatment options with their physician. It has been demonstrated that low functional health literacy is associated with sub-optimal use of health care services [174], and the association between educational level and health literacy is well documented [175]. Studies have documented that patients with higher levels of education or SES are more willing or capable to participate in shared decision-making, and that patients with lower levels of education prefer a more passive collaborative role [36, 176, 177]. Patients in different SES groups may have different preferences for whom they prefer to consult in the health care system [47]. Low SES patients might prefer to communicate with their GP rather than a specialist. The relationship with the GP might be an important factor for the communication. High SES patients might prefer to consult a specialist, as the specialist possesses special knowledge about the patient's condition [154]. Such differences in preferences might be associated with the degree of health literacy.

However, patients' willingness to participate or communicate may also reflect the physician's consulting and communication style. Physicians may presume that patients with low SES are less intelligent, less responsible, less rational and less likely to comply with medical advice [37]. This may affect the treatment decisions of the physicians [38]. The admitting physician may have a lower threshold for admitting children from families in lower SES groups, and the referring physician may have a lower threshold for referring AF patients in higher SES groups to ablation treatment. This is in accordance with our findings of a higher probability for admission and lower cost for children of parents with low level of education, and with higher ablation probability in higher SES groups. Such decisions may not be rational and fact-based, but rather reflect unrecognised assumptions about people with a different background and SES than the physicians.

5.2.4 SES as explanation of geographic variation

More than 50 years ago Julian Hart defined the 'inverse care law', to describe how people who most need health care are least likely to receive it [178]. The hypothesis is that areas with high needs, i.e., areas of high socio-economic deprivation, have poorer availability of good medical care [178]. The observed geographic variation in this thesis might be due to differences in needs between the hospital referral areas, i.e., because of differences in SES between the hospital referral areas. We therefore wanted to investigate whether the differences in health care utilisation between the hospital referral areas could be explained by differences in SES between the hospital referral areas.

In order to investigate whether SES could explain the geographic variation, multilevel analysis with random intercept for the geographic areas was applied in paper I and in the additional analysis of paper III (see table 3 in paper I and table 1 in this thesis). Multilevel analysis was not conducted in paper II, as SES gradients mainly were non-consistent. The multilevel analysis showed that the differences in SES only explain a negligible part of the geographic variation. In our studies, we found consistent SES gradients across all the hospital referral areas, independent of the level of utilisation. In paper I this consistency was true for medical hospital admissions in general (see figure 3 in paper I), and also for almost all hospital referral areas for the four sub-samples of admissions (see figure S3 in supplementary of paper I). The additional analysis of paper III also found consistency across almost all hospital referral areas, stratified by income and education and by gender (see figure 2 in this thesis).

Multilevel analysis is applied when there is reason to believe that patients nested in the same geographic area are more likely to function in the same way than patients nested in different geographic areas. In order to assess whether socioeconomic differences could explain the geographic variation, we compared the variance components of the random intercept in the empty multilevel model with the multilevel model with SES variables as covariates. If the variance components are equal, then there is no effect of adjusting for SES and therefore SES does not explain the geographic variation. In all the analyses the variance components were small, i.e., indicating that only a small fraction of the observed geographic variation was due to properties at the area level. The comparisons of variance components in the empty models with the models with SES as covariate showed very small differences. We therefore concluded that differences in SES could not explain the geographic variation, neither for hospital admissions for children nor in the probability of ablation, and we reported the result from the ordinary models.

Our results are in contrast with some studies. Both Kinge et al. and Kravdal et al. studied the role of SES on geographic variation in Norway, and they found that 50 to 80% of the geographic variation can be explained by differences in SES [60, 61]. However, in contrast to our studies, these studies are based on ecological measures of SES. Ecological SES measures have been found to be sub-optimal [62]. Kravdal et al. also applied individual data on SES, and found that SES on individual level hardly explained anything of the geographic variation [60]. One of the major strengths of the studies in this thesis is the use of data on individual level. When data on individual level are not available, ecological measures on area level are often used as proxies. Studying area differences in average outcomes may produce misleading information and incorrect conclusions [179, 180]. The use of area level measures can lead to both over- and underestimation of the association between SES and health outcomes [181]. The variation in SES on an individual level will always be larger than on an area level, and this misclassification causes underestimation of the association between SES and health outcomes. However, if there are other area specific factors than SES that independently affect the health outcomes, the association will be overestimated [182].

The positive SES gradient in ablation probability found in paper III might be interpreted as evidence for the inverse care law, and this is in line with the interpretation in other Norwegian studies [10, 183]. However, as the geographic variation could not be explained by differences in SES between the hospital referral areas, it can be questioned whether our findings in paper III supports the inverse care law. The inverse care law was mainly defined for health care systems where the supply of medical care is exposed to market forces, and less for universal health care systems such as in Norway [178].

5.2.5 The SES gradient depends on the type of health service

Socioeconomic gradients were found in all three papers, but not pointing in the same direction. Hospital admissions for children, cancer patient pathways and ablation of atrial fibrillation represent vastly different types of health care services. In paper I, the probability for a child being admitted increased with decreasing parental education. On the other hand, in paper III, the probability for ablation increased with increasing income and education. In paper II, we found that the proportion of cancer patients included in CPPs increased with income, while we were not able to document a socioeconomic gradient for CPP patients without the cancer diagnosis.

A review study found that low socioeconomic status is associated with lower access to treatment for coronary heart disease [184]. Moreover, Fiva et al. document that highly educated individuals utilise high quality cancer treatment options to a greater extent than less educated patients, and the use of

such treatment improved these patients' survival [185]. In a recent OECD study, cancer screening was less frequently participated in by those with lower income [48]. Other studies have found a negative SES gradient in utilisation of health services with a low level of specialisation [4, 6, 10, 48], and a positive SES gradient in utilisation of health services with a high level of specialisation [3, 47, 48]. A recent review study on socioeconomic inequalities in primary-care and specialist physician visits concludes that the existence of socioeconomic differences in health care utilisation heavily depends on the health services analysed [28].

Based on this, and the findings in paper I-III, one might argue that there are socioeconomic differences in utilisation of health care and that the socioeconomic gradient is related to the degree of specialisation of the health care services. The sign of the socioeconomic gradient seems to depend on the degree of specialisation of the health service of interests. Paper III covers the most specialised service, and paper I covers the least specialised service.

5.2.6 Explaining and assessing unwarranted variation

In this thesis, both geographic and socioeconomic variation has been explored, and socioeconomic status could not explain the geographic variation in either admission of children or ablation of atrial fibrillation. The challenge of how to best explain why variation exists and how to distinguish between warranted and unwarranted variation remains, as does the question of how the issues that seem inherent in such differences should be addressed.

In a recent study by Cutler et al. [49], physicians are classified as either 'cowboys' with preference for aggressive medical interventions or 'comforters' with preference for more conservative actions, based on their judgement of different clinical scenarios. They conclude that the largest degree of residual variation appears to be explained by differences in physicians' beliefs about the efficacy of particular therapies. The physicians in the study by Cutler et al. had markedly different views about how to treat the same patients. These views were often inconsistent with evidence-based professional guidelines for appropriate care [49].

In the Auditor General report on reasons for variation in utilisation of three health care services (hospital admissions for children, acromion resections and gynecological ultrasound examinations) in Norway [67], results from interviews with clinicians, both paediatricians and orthopaedists, are presented. The interviews reveal three factors that influence the clinicians' practice and thereby contribute to unwarranted variation; i) lack of consensus about best practice, ii) capacity and iii) how

fast new knowledge influences the clinicians' practice. In interviews with paediatricians from the areas with the highest and lowest admission rates for children, all the paediatricians claimed to focus on avoiding unnecessary admissions. Paediatricians in the area with the lowest admission rates stated that avoiding unnecessary admissions is a hospital policy. In the area with highest admission rates, the total care for the child and the child's relatives are emphasised when the paediatricians consider admission. They state that it can be good patient care to provide relief and reassurance through an admission even if the admission is not medically necessary. The interviews also reveal that the ability to adapt when new knowledge or new techniques emerge depends on the clinicians, and the number of clinicians and the degree of research orientation is of importance [67].

In a longitudinal study, Norwegian physicians were asked whether a patient's socioeconomic status should impact in decisions about treatment in medical care [186]. The study showed that physicians are increasingly willing to consider patients' socioeconomic factors in clinical care. Physicians are willing to spend more time on patients in lower SES groups, and the GPs were significantly more influenced by the patients' SES than other specialists. An increasing number of physicians agreed that equality of care should be understood in terms of outcomes, rather than input, i.e., physicians agreed that different amounts of resources should be used to obtain similar health effects depending on the patients' SES.

According to the definitions of warranted and unwarranted variation by both Wennberg and Sutherland, variation is warranted if it is caused by differences in the preferences of informed patients, differences in clinical practice due to innovations or new models, and differences in skill-mix or resources available between the health care providers due to adaption [12, 53]. In order to assess whether the observed variation is warranted or unwarranted, data on the above-mentioned factors is needed. Such data were not available for this thesis, and probably impossible to collect in any study, and we are therefore not able to make absolute statements about the observed variation.

In the discussions in the papers of this thesis, we tend to conclude that the observed variation is unwarranted and that clinical practice and provider preferences are important causes for both geographic and socioeconomic variation. There are known differences in the number of hospital beds per capita for children between the hospital referral areas in Norway, and there are differences in ablation capacities between the health regions in Norway. Unfortunately, we were not able to get reliable data on capacities for the analyses. However, it is reasonable to assume that the observed geographic variation is not solely due to capacity differences. There is one ablation centre in each

health region in Norway, still we find substantial variation in the ablation rate between the hospital referral areas within each health region. The proportion treated with ablation was almost seven times higher among patients in the high SES group compared to patients in the low SES group across the hospital referral areas within one single health region (Bergen vs Stavanger in West RHA, males and income, see Figure 2).

If the health status, the needs and the patient preferences in different socioeconomic groups were equal, then we could easily conclude that the observed variations between socioeconomic groups are unwarranted. However, the socioeconomic gradient in health is well known, still we argue that the observed variation is unwarranted. The observed variation in the three papers across SES groups is substantial, and probably larger than the expected differences that may be caused by differences in health or morbidity. In addition, the consistency of the socioeconomic gradients across the hospital referral areas, speaks for other explanations than differences in needs and capacity. Still, our characterisation of the variation as unwarranted is based on assumptions, because of lack of data to adjust for differences in health status, needs and patient preferences.

The drivers and causes of variation are complex, and there is no single explanation to the observed variations revealed in this thesis. It is not possible to be definitive about all the reasons for unwarranted variation because the delivery of health care services is complex, and it is not possible to control all the variables or 'moving parts' involved. The results and conclusions from studies aiming at decomposing the demand and supply side factors of geographic variation are divergent. Using Norwegian data and studying migration, Godøy et al. finds that the importance of the demand and supply side are roughly equal [57]. In a study on preventable hospitalisations in Australia, Falster et al. find that demand side factors, such as personal sociodemographic and health characteristics, are the major drivers [187]. However, most studies conclude that the supply side, i.e., properties of the health care service, is the major driver of geographic variation [49].

Cutler et al. concludes that physicians' beliefs and choices are the most important driver of variation [49]. The panel survey of physicians revealed that Norwegian physicians believe that socioeconomic factors should be considered because they influence patients' ability to benefit from medical care [186]. According to the framework of Sutherland et al.; variation can be warranted because of clinical decisions to meet the needs of patients [53]. However, as Sutherland et al. further states, if decisions are based on non-clinically relevant patient characteristics, such as SES, variation can be considered unwarranted. Whether variation is defined as warranted or unwarranted depends on how 'need' is

interpreted. Bringedal et al. proposes that 'need' should be interpreted in terms of possibilities of equal outcomes of treatment [186].

In this thesis both geographic and socioeconomic variation were found, and the geographic variation could not be explained by differences in SES. In addition, we found different SES gradients for different health care services. This may indicate that the sign of the gradient depends on the degree or level of specialisation of the service. However, we have not been able to explain the causes of variation, and we are only able to make assumptions about whether the variation is unwarranted or warranted. In a recent article by Atsma et al. [188], alternative hypotheses for mechanisms underlying unwarranted variation in health care and new target points for research to better understand, reduce and improve unwarranted variation are proposed. They propose that research focus should be on the complex cohesion of network effects, reflective medicine, patient beliefs and objective criteria for treatment choices. They conclude that this will only work if physicians themselves acknowledge the presence of unwarranted variation and are ready to initiate change.

Over-diagnosis and over-treatment are increasingly discussed as a significant problem in health care. In 2002 BMJ published an article with the title; "Too much medicine?" asking whether medical inputs at some point will produce more harm than good [189]. In 2015, the BMJ launched a digital theme issue on over-diagnosis. The Choosing Wisely Campaign was launched in 2012 by the American Board of Internal Medicine Foundation. Choosing Wisely is focused on supporting conversation between physicians and patients about whether health care is truly necessary [190]. The campaigns' mission is to promote conversation between physicians and patients to help patients choose health care that is; i) supported by evidence, ii) not duplicates of other tests or procedures already received, iii) free from harm, and iv) truly necessary. The decision of care should be based on shared decision-making (SDM). SDM has been defined as: "an approach where clinicians and patients share the best available evidence when faced with the task of making decisions, and where patients are supported to consider options, to achieve informed preferences" [191]. SDM is a joint process in which a health care professional works together with the patient to reach a decision about care. The goal of SDM is to ensure that the patient understands the risks, benefits and possible consequences of different options through discussion and information sharing.

The Choosing Wisely campaign is now established in more than 20 countries. Partly based on the reported unwarranted variation in health care utilisation in the Norwegian Health Care Atlases, the Choosing Wisely Norway Campaign was launched in 2018 by the Norwegian Medical Association

[192]. In Norway, paediatricians and radiologists have indicated that 15-20% of medical practice is over-treatment [192], and similar estimates are found in the US and Canada [193, 194]. In a survey study among more than 2000 physicians in the US, the physicians reported that more than 20% of overall medical care was unnecessary [195]. The most commonly cited reasons for over-treatment were fear of malpractice and patient pressure/request.

Primary, the Norwegian campaign was aimed at health professionals, with recommendations to physicians of things not to do and information on resources on SDM for clinicians. In 2021, Choosing Wisely Norway launched a new campaign "More is not always better", aimed at the population. In this campaign patients are encouraged to ask four questions; i) do I need this test/treatment?, ii) what are the risks and adverse events?, iii) what happens if I do nothing?, and iv) are there alternatives?. These two campaigns can lead to network effects, more reflections of diagnostic workup and treatment and patients will be more involved in the decision-making process, and thereby hopefully contribute to reduce both geographic and socioeconomic variation. Initiatives like "Choosing Wisely" and "More is not always better" might contribute to reduce unnecessary tests and treatments, to reduce clinical practice variation, to improve the patient-physician communication and to increase patient awareness and knowledge. All of this can in turn contribute to reduce both geographic and socioeconomic variation.

Research has shown that the social determinants of health (SDH) play a greater role in shaping population health than health care services [196]. The Marmot Review propose a new strategy to reduce health inequalities [197]. The Review argues that, instead of the traditional policy of focusing on solving health inequalities within the health care system, action is needed across all the social determinants of health. Key to Marmot's approach to addressing health inequalities is to create the conditions for people to take control of their own lives. This requires action across the social determinants of health and is beyond the reach of the health care system. This includes education, occupation, income, home and community [197].

6 Conclusions

The aims of this thesis were, using individual level administrative registry data, to explore geographic and socioeconomic variation in utilisation of three health care services in Norway, and to investigate whether geographic variation can be explained by differences in socioeconomic status on individual level. Both geographic and socioeconomic variation were found in all three health care services, and the variation has been characterised as unwarranted. The largest variations were found in hospital admissions for children and in ablation for atrial fibrillation. The geographic variation could not be explained by differences in socioeconomic status between the geographic areas, neither in hospital admissions for children nor in ablation for atrial fibrillation.

A negative socioeconomic gradient was found in hospital admissions for children, i.e., children of parents with low level of education were more likely to be admitted to hospital than children of parents with high level of education. The negative socioeconomic gradient in hospital admissions was consistent in all the hospital referral areas. A positive socioeconomic gradient was found, in income only, in the probability of being included in cancer pathways for cancer patients, while no consistent socioeconomic gradient was found for the proportion of cancer pathway patients diagnosed without cancer. A positive socioeconomic gradient was found in the proportion of atrial fibrillation patients treated with ablation, i.e., the probability of ablation increased with increasing level of education and income. This positive socioeconomic gradient, in both education and income, was consistent across all the hospital referral areas.

7 Final remarks and future perspectives

Both geographic and socioeconomic variation were identified for all three considered health care services. We have discussed the drivers of geographic and socioeconomic variation, both in the thesis and in the papers. Utilisation of health care services depends on a multitude of factors, some within and some outside the health care service. The variation documented in this thesis, and in many other studies, challenges the idea that medical practice and care is rational and evidence-based. Therefore, in search of explanations one must also study the impact of personal beliefs and preferences in both patients and physicians, local traditions and clinical practice, capacity, and incentives. We do not believe that all variation, but probably a significant part of the variation, is due to factors on individual level, i.e., both physicians and patients. Cutler et al. showed that geographic variation appears to be explained by differences in physicians' beliefs about the efficacy of particular therapies [49], clinical practice and differences between individual physicians might be a driving factor of geographic variation also in Norway. The association between the individual patients' level of SES and utilisation of health care services seems to be more obvious. Measures in order to reduce socioeconomic variation must therefore be aiming at levelling the playground between the SES groups.

In 2021, The Norwegian Medical Association adopted a resolution on social inequality in health [198]. The goal is to reduce social inequality in health by investigating the role of physicians and the health care system. The resolution states that different efforts are required to provide equality of care. This means, among other things, giving the most to those who need it the most, and adjusting information, examination, and treatment to the patients' need. The Geneva Declaration states that it is the physician's duty to treat equal patients equally, regardless of social standing, age, gender, disease or disability, and ethnicity [199]. Therefore, treating patients differently on the basis of their SES could be in conflict with medical ethics and also the Norwegian health policy. The white paper on priority setting in the Norwegian health care sector states that the population must have equal access to health care services. Similar cases must be treated in the same way, regardless of social status and other patient characteristics [1]. However, according to the white paper on priority setting, medical care decisions should be based on the basis of three priority-setting criteria; the benefit criterion, the resource criterion and the severity criterion [1]. Bærøe and Bringedal argue that ignoring SES can lead to preservation or reinforcement of the social inequalities in health [200]. They argue that equitable health care requires considerations of the impact of SES on patients' capacity to benefit from the care, e.g., allocating more time to patients with low SES. Both Bærøe and Bringedal and the Norwegian Medical Association resolution argue that the concept of medical fairness should be adjusted according

to this [198, 200]. The resolution focus on health literacy and patient-doctor communication among the physicians. Implementation of the resolution may therefore contribute to reduced social inequality in health, and even reduced socioeconomic and geographic variation. However, as shown by Cutler et al., different physicians may offer the same patient widely different treatments, and often not based on available evidence [49]. Therefore, implementation of the resolution should be monitored, as it may also contribute to increased variation.

The variation demonstrated in this thesis and the possible explanations should be assessed at all levels of health care management, also on the individual physician level. Many clinical decisions are not evidence-based, but rather reflect unrecognised assumptions and personal preferences. The fact that clinical practice is not entirely rational and evidence-based needs to be acknowledged at all levels of the health care system and also by physicians and patients. Especially, acknowledgement is needed among physicians about the fact that patients might respond and communicate differently depending on their background or social status, and that this might influence the decision of care.

The results in this thesis are based on "world-class" administrative data; data on individual level with high quality and on complete populations. Still, we have not been able to be definitive about the reasons for unwarranted variation, and we were not able to "explain" geographic variation by differences in SES. We are not even able to define the variation as warranted or unwarranted without making assumptions. This might be disappointing, but as the field of variation in health care utilisation is complex, also other methods and other types of data are needed to better understand the processes causing variation. Quantitative studies based on administrative data can contribute to further confirmation of variation. However, in order to get broader insights in the different processes causing variation, also qualitative studies are needed. Studies investigating patient preferences and how patients and physicians communicate and interact, studies on prejudices in physicians, and studies on how to improve health literacy in patients are warranted. Also studies on the development of clinical practice and differences in clinical practice between hospitals, departments and physicians are needed. These types of "within health care" studies can contribute to understand variation. However, to reduce social inequalities in health, also measures outside the health care system are needed.

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Paper I

BMJ Open

Impact of parents' education on variation in hospital admissions for children: a population-based cohort study

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ABSTRACT

Objectives To assess the impact of parental educational level on hospital admissions for children, and to evaluate whether differences in parents' educational level can explain geographic variation in admission rates.

Design National cohort study.

Setting The 18 hospital referral areas for children in Norway.

Participants All Norwegian children aged 1–16 years in the period 2008–2016 and their parents.

Main outcome measures Age- and gender-adjusted admission rates and probability of admission.

Results Of 1 538 189 children, 156 087 (10.2%) had at least one admission in the study period. There was a nearly twofold (1.9) variation in admission rates between the hospital referral areas (3113 per 100 000 children, 95% CI: 3056 to 3169 vs 1627, 95% CI: 1599 to 1654). Area level variances in multilevel analysis did not change after adjusting for parental level of education. Children of parents with low level of education (maternal level of education, low vs high) had the highest admission rates (2016: 2587, 95% CI: 2512 to 2662 vs 1810, 95% CI: 1770 to 1849), the highest probability of being admitted (OR: 1.18, 95% CI: 1.16 to 1.20), the highest number of admissions (incidencerate ratio: 1.05, 95% CI: 1.01 to 1.10) and admissions with lower cost (−0.5%, 95% CI: −1.2% to 0.3%).

Conclusions Substantial geographic variation in hospital admission rates for children was found, but was not explained by parental educational level. Children of parents with low educational level had the highest admission probability, and the highest number of admissions, but the lowest cost of admissions. Our results suggest that the variation between the educational groups is not due to differences in medical needs, and may be characterised as unwarranted. However, the manner in which health professionals communicate and interact with parents with different educational levels might play an important role.

Strengths and limitations of this study

- A complete national population cohort of children, both admitted and non-admitted, and their parents was studied, eliminating selection bias.
- Individualised time-dependent data eliminate measurement errors and ecological fallacies.
- A study period of 9 years ensures robust results.
- Information about the parents' income and occupational status was not available for this study.
- Reliable prevalence data at the population level on the morbidity in childhood are unavailable in Norway.

INTRODUCTION

Studies on geographic variation in healthcare utilisation started with Glover in 1938, who found large geographic variation in rates of tonsillectomy among English school children.[1] In 1973, Wennberg and Gittelsohn published similar findings in the USA.[2] Geographic variation in healthcare utilisation for children and adults has later been described independently of how healthcare delivery is organised.[3–5]

While variation has primarily been studied in the context of geographic differences, it also exists related to differences in socioeconomic status (SES). SES is the social standing or class of an individual or a group, and is often measured as a combination of education, income and occupation. If variation cannot be explained by differences in patient needs or patient preferences, it may be considered unwarranted.[6] An inverse association between SES and hospitalisation for children has been documented.[7 8] Variation between SES groups may reflect differences in disease prevalence or needs due to lifestyle or environmental factors, but may also be related to other factors, such as different doctor–patient communication.[9–11]

Norway provides free access to healthcare independent of income and SES within a single-payer publicly owned healthcare system. The health of Norwegian children is excellent with an under-five child mortality rate of 2.5 per 1000 live births in 2018 compared with 6.5 in the USA.[12] Nonetheless,

the Norwegian Child Healthcare Atlas published in 2015[5] and the Neonatal Healthcare Atlas published in 2016[13] found relatively large geographic variation between hospital referral areas in admission rates and rates of treatment procedures. This variation could not be explained by differences in morbidity or patient preferences. Higher admission rates are not necessarily associated with better outcomes[14] and may expose patients to risk of complications from treatment or hospital-acquired infections. In general, children should only be admitted to hospital if outpatient care cannot be provided with an equal or better outcome.

Using national registers, the paediatric cohort of children aged 1–16 years in Norway over a 9-year period was matched with parental educational attainment. This is the first study with individual data on a complete national cohort of children, both hospitalised and non-hospitalised, and their parents' educational level. Parental educational level was used as measure of SES.

The aim of this population-based study was to describe geographic variation and explore the effect of parental educational level on hospital admissions for children. We address the following questions: Can geographic variation in admission rates for children between hospital referral areas be explained by parental educational level? What are the impacts of parental educational level on whether a child is admitted to hospital or not? If a child is admitted, does parental educational level impact the number of admissions, disease severity and cost of admissions?

MATERIALS AND METHODS

Study design and data sources

The study population was defined using combined data from the Norwegian Patient Register (NPR) and Statistics Norway (SSB) and included a complete cohort of all Norwegian children aged 1–16 years from 1 January 2008 to 31 December 2016. Data were linked by an encrypted serial number derived from the unique 11-digit personal identifier held by all persons living in Norway. The data from SSB consisted of parental level of education each year, number and birth year of siblings, year of birth of the parents, gender and year of birth and residential municipality. The data from NPR consisted of patient demographics (residential information, age and gender), start and end date for the visit, name of hospital, type of visit, diagnoses and procedures performed. In Norway, all hospitals submit data to NPR for registration and reimbursement purposes.

Definitions

Hospital admissions for medical diagnoses (non-surgical diagnosis-related group (DRG) grouping) of at least 1 day were included in the analysis. In addition, admissions with certain primary diagnoses not considered paediatric medicine were excluded (for a detailed list of diagnoses, see online supplemental file 1). Admission episodes with less than 8 hours in between department stays were considered as one admission. Admissions that consisted of two or more department stays were registered as medical visits if all stays were registered with a medical diagnosis. Admissions were registered by the year of discharge. In addition, four subsamples of admissions were defined using primary and secondary diagnosis codes: gastroenteritis, viral and bacterial infections (excluding gastroenteritis), epilepsy and asthma (for details, see online supplemental file 1).

Parental educational level was coded using the international standard classification of education. Larger numbers represented higher educational level; 0 indicated less than primary education and 8 indicated a doctorate or equivalent, while 9 was not classified and regarded as missing. Educational level was recoded into three categories: low (0–2), medium (3–5) and high (6–8). The number of siblings was computed each year according to birth year, and analysed as a dichotomous variable; only child or child with siblings.

Statistical analyses

Data were analysed using SAS V.9.4 (SAS Institute, Cary, North Carolina, USA). The data were structured as one record per child per year, and the variables were time-dependent.

Age- and gender-adjusted admission rates were calculated for children with medical admissions in the hospital referral areas corresponding to the geographic areas served by the 18 Norwegian hospital trusts. The direct method of standardisation was applied, with three age groups (1–3, 4–9 and 10–16 years). Both annual and overall rates for the period 2008–2016 were calculated separately for parents' educational level categories. The reference population was the annual average of all children aged 1–16 years in Norway in the period.

Independent variables included were child's age and gender, maternal age, maternal and paternal level of education (categorical) and being an only child or not. Due to the high correlation between parents' ages, father's age was not included in the analysis. Restricted cubic splines (4 knots) for age with interaction terms for gender were applied, to adjust for child's age and gender. High level of education and only child were set as reference categories. In any particular analysis, observations with relevant missing data were excluded.

Admission was a dichotomous variable for each child, and the year of the first admission was used as admission time point. For children with multiple admissions, only the year of the first admission was considered. Admission was analysed using discrete-time survival analysis (based on binary logistic regression).[15]

In the analysis of the number of admissions, and the cost or severity of the admission, the study population was restricted to children with admissions only, and the independent variables were defined by the year of the first admission. The number of admissions was counted for each child in the year of the first admission. As the number of admissions is a counter variable with values

Table 1 Characteristics of children (1–16 years)* in Norway, 2008–2016

Number of children (% admitted)	1 538 189	(10.15)
Child's age, mean (SD)	6.16	(5.19)
Boys, n (%)	789 635	(51.34)
Mother's age, mean (SD)	35.81	(6.83)
Missing, n (%)	7643	(0.50)
Father's age, mean (SD)	38.87	(7.59)
Missing, n (%)	39 457	(2.57)
Mother's education ISCED, mean (SD)	4.7	(1.73)
Father's education ISCED, mean (SD)	4.48	(1.70)
Mother's educational level, categorical		
Low, n (%)	261 226	(16.98)
Medium, n (%)	488 739	(31.77)
High, n (%)	703 200	(45.72)
Missing, n (%)	85 024	(5.53)
Father's educational level, categorical		
Low, n (%)	267 667	(17.40)
Medium, n (%)	644 727	(41.91)
High, n (%)	515 724	(33.53)
Missing, n (%)	110 071	(7.16)
No of siblings, mean (SD)	1.53	(1.27)
Missing, n (%)	4 697	(0.31)
Only child, n (%)	282 498	(18.37)

*Based on the start of the follow-up for each child.
ISCED, international standard of classification of education.

greater or equal to 1, truncated negative binomial regression was applied. DRG-weight of the first admission was used as a measure of cost and disease severity. DRG-weight was analysed with linear regression. DRG-weight was highly right-skewed and was therefore log-transformed. Also, the sum of DRG-weights in the first year with admission and sum of all DRG-weights throughout the period were calculated and analysed.

To control for the impact of parental level of education on geographic variation, we conducted sensitivity analyses, that is, multilevel analysis with random intercept for the hospital referral areas. This was done for the survival analysis of admission and DRG-weight. The analyses were stratified by gender and performed with restricted cubic splines (4 knots) for age. The full model with all the independent variables was compared with a reduced model without parental education.

RESULTS

A total of 1 538 189 children were included in the analysis with a total of 8 946 984 entries over the study period (2008–2016). Of these, 156 087 (10.2%) children had at least one admission (table 1). There were 198 293 admissions during the year of the first admission, with

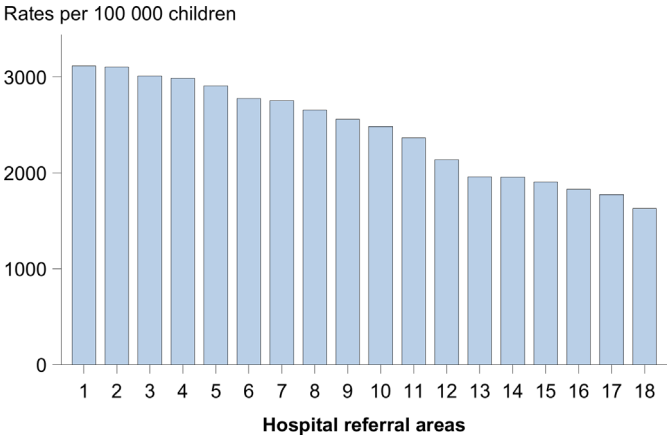

Figure 1 Age- and gender-adjusted hospital admission rates per 100 000 children, by hospital referral areas, average total rates.

an average of 1.27 (SD: 1.12) admissions per child. The mean DRG-weight for the first admission was 0.76 (SD: 0.59).

There was a near twofold (1.9) difference in admission rates between the hospital referral areas (area 1: 3113 per 100 000 children, 95% CI: 3056 to 3169 vs area 18: 1627, 95% CI: 1599 to 1654) (figure 1 and online supplemental table S1). Admission rates increased as the level of education for both the mother and father decreased. The effect was consistent with a slight decrease in overall admission rates over time (figure 2 and online supplemental table S1). Children of mothers with low level of education had on average 36% higher admission rates compared with children of mothers with high level of education (in 2016: 2587, 95% CI: 2512 to 2662 vs 1810, 95% CI: 1770 to 1849). The same pattern was found in all hospital referral areas independent of total admission rates in each area (figure 3 and online supplemental table S1). The results from the analyses of the subsamples of admissions were similar (online supplemental figures S1–S3).

In the analyses adjusted for other factors, the probability of admission increased with decreasing maternal

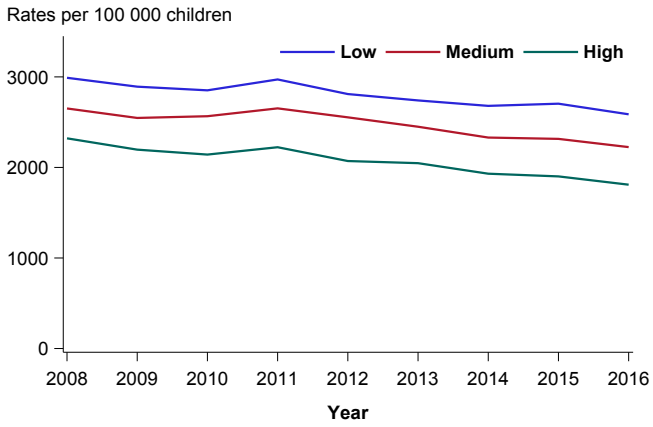

Figure 2 Age- and gender-adjusted hospital admission rates per 100 000 children, annual rates, by mothers' educational level.

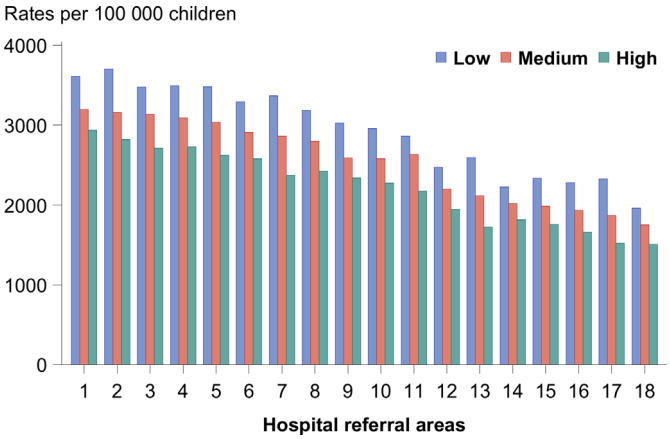

Figure 3 Age- and gender-adjusted hospital admission rates per 100 000 children, average rates, by hospital referral areas (sorted in the same order as figure 1) and mothers' educational level.

and paternal level of education (low vs high maternal level of education—OR: 1.18, 95% CI: 1.16 to 1.20; low vs high paternal level of education—OR: 1.21, 95% CI: 1.19 to 1.23) (table 2). The probability of admission decreased with increased maternal age (per 5 years—OR: 0.94, 95% CI: 0.93 to 0.94) and being an only child (OR: 0.91, 95% CI: 0.90 to 0.93). Results from multilevel analysis were similar (table 3). Multilevel analysis without parental level of education (the reduced model in table 3) resulted in similar area-level variance, indicating that differences in parental level of education do not explain the geographic variation and vice versa. Analysis stratified by children's age also found a negative parental educational gradient for almost all ages. In addition, in the analyses of the subsamples the negative educational gradient was found (online supplemental table S2).

Children of parents with low or medium level of education had a higher number of admissions than children of parents with a high level of education (incidence rate ratios (IRRs): 1.05, 95% CI: 1.01 to 1.10), low vs high paternal level of education (IRR: 1.05, 95% CI: 1.01 to 1.09) (table 2). The number of admissions per child increased with maternal age (per 5 years—IRR: 1.03, 95% CI: 1.02 to 1.05).

DRG-weight was highest for children of parents with high level of education. The differences from the reference category were <2% and mostly statistically significant (low vs high maternal level of education (−0.5%, 95% CI: −1.2% to 0.3%), low vs high paternal level of education (−1.9%, 95% CI: −2.7% to −1.1%)). DRG-weight increased with maternal age (per 5 years—1.2%, 95% CI: 0.9% to 1.4%), while being an only child was associated with a lower DRG-weight (−1.1%, 95% CI: −1.8% to −0.3%) (table 2). Applying the two alternative measures for cost also resulted in the highest sums of DRG-weights for children of parents with high level of education. The results from the multilevel analysis were similar (table 3).

DISCUSSION

Principal findings

Children of parents with low level of education had the highest admission rates, while children of parents with high level of education had the lowest admission rates. This was consistent both over time and across hospital referral areas. The geographic variation in admission rates was nearly twofold but was not explained by differences in parents' level of education. The analyses based on individual data from all Norwegian children aged 1–16 during 2008–2016 (table 2) supported the results from the ecological analyses of admission rates (figure 3).

Table 2 Factors associated with admission, number of admissions and DRG-weight, determined by multiple regressions, with 95% CIs

Covariate	Category	Admission (OR)*	Number of admissions (IRR)†	DRG-weight (%)‡
Mother's age	Per 5 years	0.94 (0.93 to 0.94)	1.03 (1.02 to 1.04)	1.2 (0.9 to 1.4)
Mother's educational level	Low	1.18 (1.16 to 1.20)	1.05 (1.01 to 1.10)	−0.5 (−1.2 to 0.3)
	Medium	1.11 (1.09 to 1.12)	1.04 (1.01 to 1.07)	−1.5 (−2.1 to −0.9)
	High	1.0	1.0	0
Father's educational level	Low	1.21 (1.19 to 1.23)	1.05 (1.01 to 1.09)	−1.9 (−2.7 to −1.1)
	Medium	1.14 (1.13 to 1.16)	1.04 (1.01 to 1.08)	−1.7 (−2.4 to −1.1)
	High	1.0	1.0	0
Only child	Yes	0.91 (0.90 to 0.93)	0.99 (0.95 to 1.02)	−1.1 (−1.8 to −0.3)
	No	1.0	1.0	0

*Survival analysis with binary logistic regression, restricted cubic splines knots for age (4,7,10,13), n=7 701 336. Adjusted effects are ORs.
†Truncated negative binomial regression, restricted cubic splines knots for age (1,3,6,12), n=1 43 697. Adjusted effects are IRRs.
‡Linear regression with log-transformed outcome, restricted cubic splines knots for age (1,3,7,12), n=1 43 664. Adjusted effects are percentage differences from the reference category (100×(exp(estimate)−1)).
DRG, diagnosis-related group; IRRs, incidence rate ratios.

Table 3 Results from multilevel analysis for admission and DRG-weight, with random intercept for hospital referral area and restricted cubic splines for age, stratified by gender. Point estimates with 95% CIs

		Admission (OR)*			
		Reduced model†		Full model	
Covariate	Category	Girls	Boys	Girls	Boys
Mother's age	Per 5 years	0.92 (0.91 to 0.93)	0.94 (0.93 to 0.94)	0.94 (0.94 to 0.95)	0.96 (0.95 to 0.96)
Mother's educational level	Low			1.20 (1.17 to 1.22)	1.17 (1.15 to 1.20)
	Medium			1.09 (1.07 to 1.11)	1.09 (1.07 to 1.11)
	High			1.0	1.0
Father's educational level	Low			1.19 (1.16 to 1.22)	1.15 (1.13 to 1.18)
	Medium			1.08 (1.06 to 1.10)	1.07 (1.05 to 1.09)
	High			1.0	1.0
Only child	Yes	0.90 (0.88 to 0.92)	0.89 (0.88 to 0.91)	0.91 (0.89 to 0.94)	0.91 (0.89 to 0.93)
	No	1.0	1.0	1.0	1.0
Random effect (logit scale)					
Area-level variance		0.046	0.041	0.043	0.039
Spline knots for age		4,7,10,13	4,7,10,13	4,7,10,13	4,7,10,14
n		4 078 653	4 250 513	3 767 811	3 933 525
		DRG-weight (%)‡			
Mother's age	Per 5 years	1.32 (0.98 to 1.67)	1.11 (0.79 to 1.44)	1.15 (0.77 to 1.53)	1.15 (0.79 to 1.51)
Mother's educational level	Low			−1.39 (−2.47 to -0.29)	0.15 (−0.89 to 1.20)
	Medium			−1.83 (−2.71 to −0.93)	−1.29 (−2.12 to −0.45)
	High			0	0
Father's educational level	Low			−1.19 (−2.34 to −0.02)	−1.37 (−2.46 to −0.28)
	Medium			−1.39 (−2.31 to −0.47)	−1.20 (−2.05 to −0.35)
	High			0	0
Only child	Yes	−0.92 (−2.05 to 0.22)	−0.67 (−1.69 to 0.35)	−1.34 (−2.46 to -0.21)	−0.86 (−1.87 to 0.15)
	No	0	0	0	0
Random effect (log scale)					
Area level variance		0.002	0.001	0.002	0.001
Residual variance		0.243	0.240	0.244	0.240
Spline knots for age		1,3,8,13	1,2,3,11	1,3,8,13	1,2,6,11
n		72 925	82 642	67 419	76 243

*Survival analysis with binary logistic regression. Adjusted effects are ORs.
†Reduced model: without parental education.
‡Linear regression with log-transformed outcome. Adjusted effects are percentage differences from the reference category (100×(exp(estimate)−1)).
DRG, diagnosis-related group.

They further indicated that children of parents with low and medium level of education also had somewhat more frequent admissions per child, while the cost or severity per admission was slightly lower for these children compared with children of parents with high level of education.

Comparison with previous studies

The geographic variation in admission rates is in accordance with the findings of unwarranted variation reported in the Child healthcare atlas for Norway.[5] Our present study found the same variation over a time span of 9 years as the 5-year duration in the atlas. The observed geographic variation in the atlas and in this study can mainly be attributed to two different mechanisms for unwarranted variation, preference-sensitive and supply-sensitive care.[6] Preference-sensitive care represents practice, preferences and beliefs of a single clinician or department rather than a clear evidence-based approach and unwarranted variation is caused by differences in clinical practice or patients' participation in care decisions. Supply-sensitive care refers to medical services for which utilisation rates are sensitive to local availability of healthcare resources, and unwarranted variation is due to differences in capacity. It is reasonable to assume that the observed variation between the hospital referral areas is related to both differences in clinical practice and differences in capacity. The inverse gradient between admission rates and parental level of education is in accordance with findings by others.[8 16 17] Similar results have also been found for adults in systems with universal healthcare coverage.[18]

DRG-weight may serve as a crude indicator of disease severity. DRG-weight was positively associated with increasing level of parental education, suggesting that the conditions causing the admission were slightly less severe among children of parents with low level of education. Previous studies have found higher treatment costs for children with low SES.[7 8 19] Nonetheless, the number of admissions was about 5% higher among children of parents with low level of education compared with children of parents with high level of education in our study. Moreover, the sum of DRG-weights in the first year with admission and the sum of all DRG-weights throughout the period for children of parents with high level of education were slightly higher than that of children of parents with low and medium level of education. The contrast with previous studies may be related to their use of ecological SES measures or SES fixed to a point in time not necessarily corresponding to the hospital admission. Unlike these studies, we used individualised paired data for each child–parent couple at the year of admission.

Possible explanations of our findings

Out-of-pocket payment or lack of health insurance may be an obstacle to disadvantaged groups seeking healthcare.[20] All healthcare for children under the age of 16 in Norway is free of charge, and parents are economically compensated for the loss of income if admitted to hospital with their child. This most likely excludes a significant effect of economic restraints on access to healthcare for children.

Thus, there must be other factors involved explaining the variation associated with education. First, there may be differences in disease prevalence and medical needs or informed preferences related to parents' level of education.

There is increasing evidence of a positive relationship between SES and health outcomes throughout the life span.[21] However, most SES factors influencing health status are related to exposure over time, during a critical period or through the pathway of learnt lifestyle. As a consequence, the major impact of SES on health becomes apparent later on in life, not during childhood.[22]

There is a paucity of reliable population-based disease prevalence data in children. Although utilisation of healthcare resources is commonly interpreted as an indicator of prevalence, this is hardly correct given the large geographic variation found by us and others.[3–5] Disease prevalence is not consistently higher in children with low SES. Atopic disease and allergies occur more frequently among children with high SES.[23–25] The prevalence of asthma did not show an association with SES, while severe asthma was most prevalent in low SES groups according to an analysis by Mielck *et al*.[26] A recent Danish study found a significantly higher risk of childhood nervous system tumours of all types among children with highly educated parents or mothers with high income.[27] A German cross-sectional study concluded that only a few health indicators such as obesity occurred more frequently in socially disadvantaged children.[25] The pattern of admission rates found in our study does not necessarily fit with the heterogeneous pattern of SES-related prevalence for diseases in childhood, and care should be taken not to interpret admission rates as a reflection of prevalence.

The majority of paediatric hospital admissions in Norway are related to acute and less-severe disease, and most children admitted are only hospitalised once or twice during childhood. The standard of living in Norway is high, income inequality is relatively small and few children live in poverty. It may therefore be questioned if variation in admission rates as large as 36% between educational groups is reasonable and if it is solely related to differences in disease prevalence.

Alternatively, the variation associated with education and SES may be related to other factors than the child's health status. Both differences in preferences and capacity may contribute to large variation in healthcare usage between geographic areas. These mechanisms are usually unintended and not recognised by providers. It may be due to attitudes or beliefs held by either parents or physicians, which may impact the decision of admission.

Finnvold found that despite the strict practice of admission criteria, children with severe asthma are more likely to be admitted to a specialised asthma hospital if their parents have higher education, participate in patient organisations or there is a physician in the family.[28] This indicates that manoeuvrability related to higher education and social capital increases the chances of admission to a specialised hospital. One of the mechanisms underlying SES differences in healthcare usage may be found in the concept of health literacy, which captures the difficulties parents may encounter in finding their way through the healthcare system.[29] Health literate parents may be more capable of understanding and discussing treatment options on equal grounds with their physician and therefore avoid admissions with little benefit over outpatient care. The association between educational level and health literacy is well documented.[30] It is demonstrated that low functional health literacy is associated with suboptimal use of healthcare services.[31]

It has been claimed that parents with higher levels of education or SES are more willing or capable to participate in shared decision-making.[9 32] Salvador *et al* found an association between parents preferring a passive collaborative role and lower levels of education.[33] However, parents' willingness to participate may reflect the physician's consulting and communication style. In a meta-analysis on doctor–patient communication related to SES,[9] physicians gave more information, more explanation, were more emotionally supportive and more often adapted shared decision-making with patients of high SES. Furthermore, patients with low SES received more physical examination. Physicians may presume that patients with low SES are less intelligent, less responsible, less rational and less likely to comply with medical advice.[10] This may affect decisions on whether to admit the child to inpatient care or not.[11] Therefore, the physician may have a lower threshold for admitting children

from families with low and medium SES. This is also in accordance with our findings that there is a higher probability for admission and lower cost for children of parents with low level of education. Such decisions may not be rational and fact-based, but rather reflect unrecognised assumptions about people with a different background and SES than the physicians.

If the variation in admission rates between educational groups does not reflect needs or informed preferences, the variation may be characterised as unwarranted. The correct rate reflects the decision of fully informed patients and families, while variation in rates reflects both local practice and the influence of physicians on parental decisions.[34] If the extent of shared decision-making increases with parental SES, the admission rate of children with higher SES may better reflect actual needs based on medical criteria and preferences.

Strengths and limitations

The strength of this study is the use of individualised yearly matched data for each child and parents' level of education, for both admitted and non-admitted children. The parental level of education in Norway increased during the study period, with a 5 percentage points increase in the proportion with high level of education. In the analyses, parental level of education in the year of the child's admission was applied. The study covered a complete national cohort of children over 9 years, with consistent findings both over time and between groups. The completeness of data eliminates selection bias.

A limitation might be that income has not been included as an indicator of SES, which may or may not improve the classification of SES. However, income is volatile and fluctuates considerably over time. Kaarbøe and Carlsen found that for hospital admissions in children under the age of 11 in Norway, the educational gradient dominated the income gradient for SES.[7] Halldòrsson *et al* found that education was a more important determinant of healthcare utilisation for children than the financial situation of the families in Nordic countries.[16]

Unanswered questions and future research

Our data did not allow firm conclusions about a causal relationship, neither between medical needs nor non-medical factors, and differences in hospital admission rates among children of parents with different educational level. Previous studies on geographic variation in medical care indicated that physician preferences exert a major impact on variation in care.[35] This may also be true for variation between SES groups, even though the nature and quality of these preferences may be different. More research on how health professionals communicate with patients of different SES and the effects on treatment decisions is needed.

The goal of shared decision-making is to improve the overall quality of clinical decisions, satisfaction and to avoid admissions with no benefit over outpatient care. However, shared decision-making depends on a two-way partnership between the physician and the parents. Parents without sufficient understanding of their child's medical condition are not able to make educated and fully informed decisions. Therefore, tools to improve health literacy among patients/parents and to increase physician's skills in communication are needed.

CONCLUSION

This population-based cohort study, including all Norwegian children aged 1–16 years, demonstrates that children of parents with low or medium level of education have an increased likelihood of being admitted to inpatient hospital care. Geographic variation in admission rates cannot be explained by differences in parents' level of education. Different admission rates do not necessarily reflect differences in disease prevalence, but may also reflect differences in interaction between the healthcare provider and the child's parents depending on the parents' level of education.

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Competing interests None declared.

Patient consent for publication Not required.

Ethics approval The study is based on secondary use of clinical administrative data. For this reason, approval from Regional Committees for Medical and Health Research Ethics (REK) is not required, but REK has given exemption from the duty of confidentiality (20627/REK sør-øst A). The project has conducted a Data Protection Impact Assessment (DPIA). Further ethical approval or obtaining informed consent was not required for this study.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data may be obtained from a third party and are not publicly available. The original data were not collected by the authors but made available by record-linkage between the Norwegian Patient Registry (NPR) and the Statistics Norway (SSB), using the unique 11 digits personal ID. Individual-level health data are, by definition, considered to be sensitive information in the Norwegian legislation, even if deidentified and strict confidentiality requirements prevent sharing of data in public repositories. According to a contract signed with the NPR and the SSB, the project is not allowed to forward data, or subsets of data, to other researchers, except project members named in the Data Protection Impact Assessment (DPIA). Furthermore, we are required to delete the linked dataset by 31 December 2023. Researchers with approval of an exemption from professional secrecy requirements for the use of personal health data in research from the

Regional Committee for Medical and Health Research Ethics (REK) would be able to create an almost identical (updated) dataset by applying to the NPR and the SSB.

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Supplementary

Detailed list of primary diagnosis (ICD-10) not considered paediatric medicine: eye diseases (H00–H59), injuries (S00–S99, T0–T3, T79, T81, T84, T87, T90–T95, T98), orthopaedics (M15–M19, M20–M25, M65–M68, M70–M79, M91–M94, M95–M99), malformations (Q10–Q18, Q30, Q68–Q74), nosebleed (R04) and observation diagnoses (Z00.4, Z00.6, Z00.8, Z01.0, Z01.2, Z01.4, Z01.6, Z01.7, Z01.8, Z04.0–Z04.8, Z09.4, Z10–Z13, Z30–Z39, Z40–42, Z44, Z46.0–Z46.8, Z47–48, Z89).

Sub-samples of admissions defined by primary and/or secondary diagnoses (ICD-10): Gastroenteritis: A08-09, R10-11. Viral and bacterial infections (excluding gastroenteritis): B00-02, B08, B15-19, B25, B27, B33-34, J02-06, J13-14, J18. Epilepsy: G40-41. Asthma: J45-46.

Table S1: Age- and gender-adjusted hospital admissions rates per 100 000 children (95% confidence interval), by mothers' educational level, annually and by hospital referral area.

Year	Low	Medium	High	Total
2008	2990 (2905 to 3076)	2651 (2596 to 2707)	2321 (2277 to 2366)	2547 (2515 to 2580)
2009	2892 (2808 to 2976)	2547 (2491 to 2602)	2197 (2154 to 2239)	2428 (2397 to 2460)
2010	2852 (2769 to 2934)	2566 (2509 to 2622)	2142 (2100 to 2184)	2399 (2368 to 2430)
2011	2972 (2889 to 3055)	2652 (2595 to 2710)	2223 (2181 to 2265)	2491 (2460 to 2523)
2012	2810 (2730 to 2891)	2553 (2496 to 2610)	2071 (2030 to 2111)	2350 (2320 to 2381)
2013	2740 (2661 to 2819)	2450 (2393 to 2506)	2047 (2007 to 2088)	2293 (2263 to 2323)
2014	2680 (2603 to 2757)	2330 (2274 to 2386)	1931 (1891 to 1970)	2188 (2158 to 2218)
2015	2704 (2627 to 2782)	2315 (2259 to 2372)	1901 (1862 to 1940)	2176 (2146 to 2206)
2016	2587 (2512 to 2662)	2225 (2169 to 2281)	1810 (1770 to 1849)	2087 (2057 to 2117)
Area	Low	Medium	High	Total
1	3614 (3470 to 3758)	3196 (3095 to 3297)	2941 (2859 to 3024)	3113 (3056 to 3169)
2	3702 (3589 to 3815)	3164 (3088 to 3240)	2821 (2757 to 2884)	3100 (3056 to 3144)
3	3478 (3320 to 3636)	3136 (3021 to 3251)	2714 (2620 to 2809)	3007 (2942 to 3072)
4	3493 (3375 to 3612)	3094 (3013 to 3175)	2732 (2665 to 2799)	2983 (2937 to 3029)
5	3481 (3324 to 3638)	3036 (2938 to 3134)	2623 (2538 to 2708)	2905 (2847 to 2963)
6	3291 (3074 to 3507)	2909 (2776 to 3041)	2580 (2477 to 2684)	2773 (2699 to 2847)
7	3369 (3236 to 3502)	2862 (2766 to 2959)	2374 (2296 to 2452)	2750 (2696 to 2805)
8	3185 (3053 to 3318)	2798 (2714 to 2882)	2424 (2357 to 2491)	2655 (2608 to 2703)
9	3026 (2817 to 3234)	2589 (2425 to 2753)	2340 (2216 to 2464)	2560 (2472 to 2647)
10	2959 (2786 to 3131)	2579 (2469 to 2690)	2274 (2185 to 2363)	2481 (2418 to 2544)
11	2862 (2766 to 2959)	2633 (2567 to 2700)	2173 (2128 to 2219)	2363 (2329 to 2397)
12	2472 (2377 to 2568)	2200 (2125 to 2275)	1945 (1882 to 2009)	2136 (2095 to 2178)
13	2595 (2475 to 2714)	2118 (2047 to 2188)	1724 (1675 to 1773)	1959 (1921 to 1996)
14	2226 (2157 to 2294)	2019 (1966 to 2072)	1815 (1772 to 1858)	1955 (1926 to 1984)
15	2332 (2240 to 2425)	1986 (1927 to 2046)	1756 (1711 to 1801)	1905 (1872 to 1938)
16	2282 (2197 to 2366)	1932 (1875 to 1989)	1663 (1625 to 1701)	1828 (1799 to 1857)
17	2330 (2201 to 2458)	1870 (1782 to 1959)	1526 (1465 to 1586)	1774 (1728 to 1820)
18	1962 (1886 to 2038)	1753 (1686 to 1820)	1505 (1471 to 1540)	1627 (1599 to 1654)

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Table S2: Factors associated with admission, number of admissions and DRG-weight, determined by multiple regressions, with 95% confidence intervals.

Covariate	**Category**	**Admission (OR)**∗	**Number of admissions (IRR)**‡	**DRG-weight (%)**†
Mother's age	Per five years	0.94 (0.93 to 0.94)	1.03 (1.02 to 1.04)	1.2 (0.9 to 1.4)
Mother's	Low	1.18 (1.16 to 1.20)	1.05 (1.01 to 1.10)	-0.5 (-1.2 to 0.3)
educational	Medium	1.11 (1.09 to 1.12)	1.04 (1.01 to 1.07)	-1.5 (-2.1 to -0.9)
level	High	1.0	1.0	0
Father's	Low	1.21 (1.19 to 1.23)	1.05 (1.01 to 1.09)	-1.9 (-2.7 to -1.1)
educational	Medium	1.14 (1.13 to 1.16)	1.04 (1.01 to 1.08)	-1.7 (-2.4 to -1.1)
level	High	1.0	1.0	0
Only child	Yes	0.91 (0.90 to 0.93)	0.99 (0.95 to 1.02)	-1.1 (-1.8 to -0.3)
	No	1.0	1.0	0

∗ Survival analysis with binary logistic regression, restricted cubic splines knots for age (4,7,10,13), n=7 701 336. Adjusted effects are Odds Ratios (OR). ‡ Truncated negative binominal regression, restricted cubic splines knots for age (1,3,6,12), n=143 697. Adjusted effects are Incidence Rate Ratios (IRR). † Linear regression with log transformed outcome, restricted cubic splines knots for age (1,3,7,12), n=143 664. Adjusted effects are percentage differences from the reference category (100*(exp(estimate)-1)).

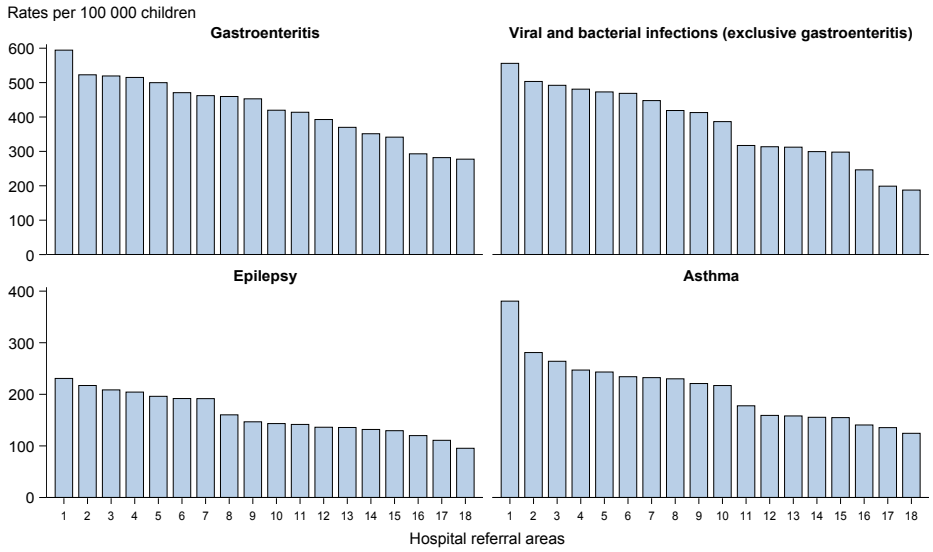

Figure S1: Age- and gender-adjusted hospital admission rates per 100 000 children for four sub-samples of admissions, average total rates, by hospital referral areas.

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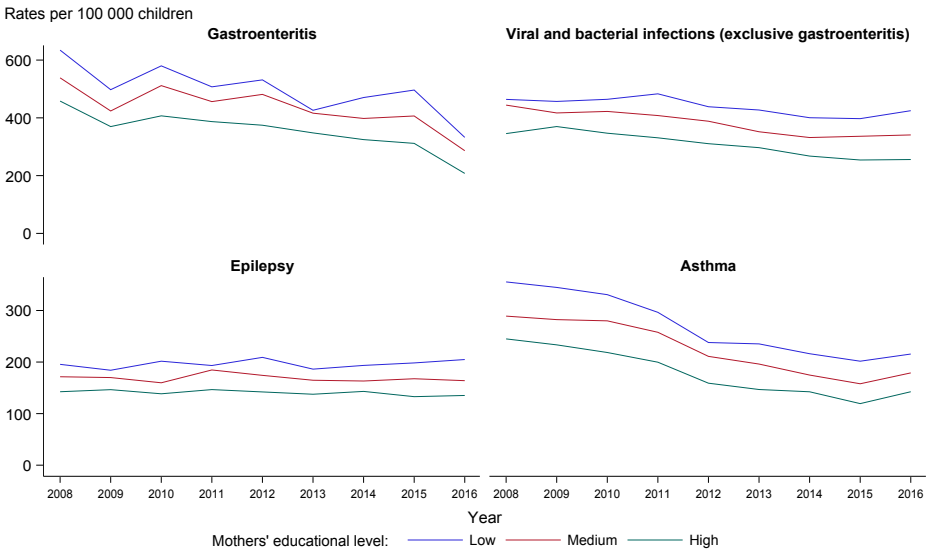

Figure S2: Age- and gender-adjusted hospital admission rates per 100 000 children for four sub-samples of admissions, annual rates, by mothers' educational level.

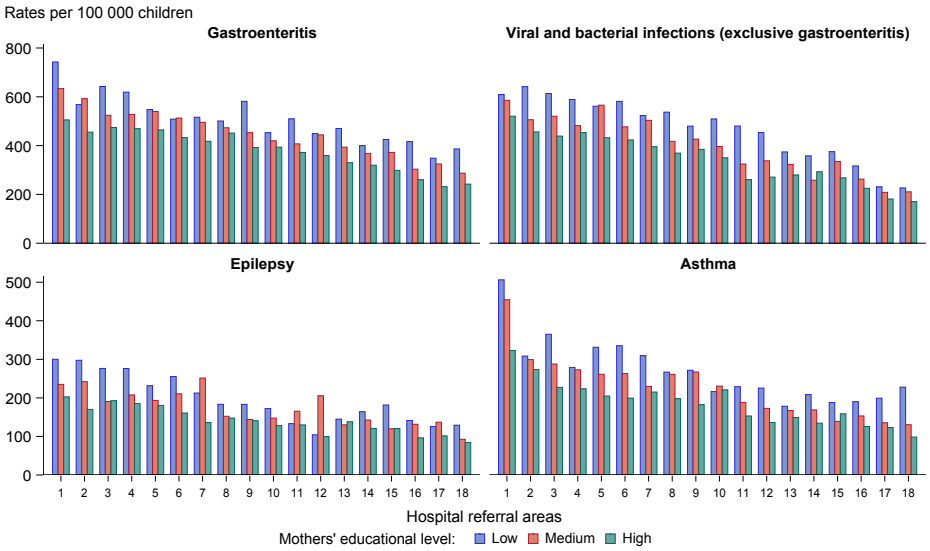

Figure S3: Age- and gender-adjusted hospital admission rates per 100 000 children for four sub-samples of admissions, average rates, by mothers' educational level and hospital referral areas.

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Paper II

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BMC Health Services Research

RESEARCH Open Access

Equitable access to cancer patient pathways in Norway – a national registry-based study

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Abstract

Background: In 2015, cancer patient pathways (CPP) were implemented in Norway to reduce unnecessary non-medical delay in the diagnostic process and start of treatment. The main aim of this study was to investigate the equality in access to CPPs for patients with either lung, colorectal, breast or prostate cancer in Norway.

Methods: National population-based data on individual level from 2015 to 2017 were used to study two proportions; i) patients in CPPs without the cancer diagnosis, and ii) cancer patients included in CPPs. Logistic regression was applied to examine the associations between these proportions and place of residence (hospital referral area), age, education, income, comorbidity and travel time to hospital.

Results: Age and place of residence were the two most important factors for describing the variation in proportions. For the CPP patients, inconsistent differences were found for income and education, while for the cancer patients the probability of being included in a CPP increased with income.

Conclusions: The age effect can be related to both the increasing risk of cancer and increasing number of GP and hospital contacts with age. The non-systematic results for CPP patients according to income and education can be interpreted as equitable access, as opposed to the systematic differences found among cancer patients in different income groups. The inequalities between income groups among cancer patients and the inequalities based on the patients' place of residence, for both CPP and cancer patients, are unwarranted and need to be addressed.

Keywords: Norway, Critical pathways, Universal health care, Cancer, Socioeconomic factors, Small-area analysis

Background

Cancer patient pathways (CPP) have been established in several countries to avoid an undesirable delay in cancer diagnosis and treatment. In the early 2000s, urgent referral pathways were introduced in the UK and in Spain, targeting an upper limit of two weeks between seeing a general practitioner (GP) to being referred to a specialist at a hospital [1, 2]. Denmark implemented CPPs in 2007–2008 [3, 4], and Sweden during the years 2015-2018 [5]. In addition to reducing and standardising waiting times, in Denmark CPPs were also intended to improve survival of cancer patients.

Norway introduced CPPs in January 2015 for lung, colorectal, breast and prostate cancers [6–9]. These cancer sites represented approximately 50% of all new cases, as well as half of all cancer-related mortality in 2016 [10]. Later in 2015, another 24 CPPs were implemented. All Norwegian CPPs were based upon Norwegian guidelines for diagnosis, treatment and follow-up of the specific cancer groups [11]. The aim was to reduce unnecessary non-medical delay in the diagnostic and start of treatment

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period and to increase satisfaction, quality and predictiveness to patients with a suspicion of cancer [12].

Patients are referred to a CPP by a GP, a specialist in private practice or a specialist in a public hospital if the doctor has a "justified suspicion of cancer" [11]. The suspected cancer diagnosis should be based on a set of symptoms and tests, described in national guidelines for CPPs [6–9], and the referral should be labelled as "cancer patient pathway". There are three possible outcomes in a CPP: the patient is diagnosed with the associated cancer, the patient is diagnosed with another type of cancer, or the patient is not diagnosed with cancer. In Norway, it is a national aim that at least 70% of all cancer patients are included in a CPP [13].

Although national criteria for inclusion in CPPs are stated clearly, the proportion of CPP patients who turn out not to have the associated cancer may still vary between hospital referral areas and subgroups of patients. High proportions of patients without the cancer diagnosis among the CPP patients may be an indication of open access or a wide funnel for inclusion into a CPP. Wide funnels into CPPs may also result in higher proportions of cancer patients included in CPPs and thus fewer cancer patients diagnosed and treated outside CPP.

The Norwegian healthcare system aims to provide equitable access to health care to all citizens, irrespective of their socioeconomic status (SES), place of residence, age, gender or ethnicity. Nevertheless, unwarranted geographic variation in health care utilisation has been documented by the Norwegian Healthcare Atlases [14] in a broad spectrum of services, in cancer treatment for the Norwegian elderly [15] and according to current official statistics [12]. Unwarranted variation is defined as differences in health care utilisation that cannot be explained by patient needs or preferences [16].

Nilssen et al. have previously studied cancer patients in CPPs in Norway [17]. However, the proportion of patients in CPPs without the cancer diagnosis, and sociodemographic factors associated with this proportion, are not known. Furthermore, the statistical relationship between the proportion of patients in a CPP without the cancer diagnosis and the proportion of cancer patients included in a CPP in Norway has not previously been studied.

The main aim of this study was to investigate the equality in access to CPPs in Norway. Based on individual data CPP patients without the cancer diagnosis and cancer patients included in CPP were studied. In addition, the relationships of patient factors such as place of residence, age, education, income, comorbidity and travel time to hospital were examined. A secondary aim was to investigate the relation between the proportion of CPP patients without the cancer diagnosis and the proportion of diagnosed cancer patients included in CPP across the geographic areas.

Methods

Study design and data sources

A national registry-based study was conducted linking data from the Norwegian Patient Registry (NPR), the Cancer Registry of Norway (CRN) and Statistics Norway (SSB). All Norwegian citizens have a unique 11-digit personal identifier that allows tracking of patients in time and between hospitals, regions and registries. Socioeconomic data from SSB were linked with the NPR and CRN data, by an encrypted serial number derived from the 11-digit personal identifier. The information from SSB consisted of yearly income and educational data. The NPR data consisted of patient characteristics (residential information, age and gender), hospital, diagnoses, and procedures. Cancer diagnosis and diagnosis date were obtained from the CRN data. All Norwegian hospitals, and all private specialists with public funding contracts, must submit data to NPR for registration and reimbursement purposes. All Norwegian cancer cases are to be reported to CRN.

The data included all Norwegian patients aged 18 years and above in CPPs for lung, colorectal, prostate or breast cancer (CPP patients) and patients diagnosed with lung, colorectal, prostate or breast cancer (cancer patients) in the period 1 January 2015 to 31 December 2017. Thus, two patient populations were analysed: i) CPP patients and the proportion without the relevant cancer and ii) cancer patients and the proportion included in the associated CPP.

Definitions

Only the first cancer diagnosis (CRN data) and the first CPP (NPR data) for each patient were considered. The pathway type in the NPR data was matched on cancer diagnosis in the CRN data and vice versa. CPP patients without the associated cancer diagnoses, i.e., patients not diagnosed with cancer at all or patients diagnosed with another type of cancer, were defined as CPP patients without the cancer diagnosis.

Educational level was coded applying the international standard classification of education (ISCED) [18]. Larger numbers represented higher education levels; 0 represented less than primary education, and 8 indicated a doctorate or equivalent while 9 was not classified and regarded as missing. Education level in the analyses was recoded into three categories; low (0-2), medium (3-5) and high (6-8), where 3-5 is high school level.

After-tax income was calculated as total income minus assessed tax and negative transfers, with total income representing the sum of income as employee, income from self-employment, property income, capital income

and transfers received. The after-tax income was index-adjusted to 2015 by the consumer price index (CPI) to account for inflation. From after-tax income a categorical income variable was defined with three categories; low (less than NOK 240 000), medium (NOK 240 000 - 400 000), high (more than NOK 400 000).

Comorbidity was measured by a modified version of the Charlson comorbidity index (CCI) [19], based on diagnostic codes (ICD-10) from hospitalisations within one year prior to the start of the CPP or the cancer diagnosis. The index was categorised into low (CCI=0), medium (CCI=1) and high (CCI>1).

The travel time by road was calculated from the patients' municipality centre to the nearest hospital, and was categorised into short (less than 30 minutes), medium (30 to 60 minutes) and long (more than one hour).

The patients' hospital referral areas were defined by place of residence and the corresponding geographic catchment areas served by the 21 Norwegian hospital trusts.

Patients with missing data on education or income, unknown place of residence or older than 90 years were excluded from the analysis (Fig. 1).

Statistical analyses

Data were analysed using SAS 9.4 (SAS Institute, Cary NC).

The analyses for both CPP patients and cancer patients were stratified by gender and CPP type or cancer diagnosis. Separate analyses were conducted for i) patients in CPP and ii) patients with cancer diagnosis, for each of the six groups: lung (males and females), colorectal (males and females), prostate and breast (females only).

Two dichotomous outcomes were analysed by logistic regressions; i) among CPP patients: the proportion without the cancer diagnosis and ii) among cancer patients: the proportion included in the CPP. The following categorical independent variables were included in the statistical model: patients' age in age intervals, level of income and education, comorbidity, travel time and hospital referral area. Age interval 60 to 69 years, high level of education and income, low comorbidity, short travel time and Akershus hospital referral area (the largest one in terms of number of patients) were set as reference categories. Wald tests were used to assess the significance of the independent variables and potential interactions. *P*-values for linear trends over categories were calculated for four independent variables; education, income, comorbidity and travel time, by separate analyses with all the other independent variables included as categorical without any assumptions of a linear trend. For main effects, p-values <0.05 were considered statistically significant. Because of the large number of potential interactions involved, interactions were considered statistically significant if p-value <0.01. However, no statistically significant interactions were observed.

The selection of the independent variables, i.e., adjusting for potential confounders and avoiding the Table II fallacy [20], was assessed in separate analyses by causal diagrams or the directed acyclic graph (DAG) methodology [21].

Age-adjusted proportions of CPP patients without the cancer diagnosis and of cancer patients included in CPP were calculated for the 21 hospital referral areas. The direct method of standardisation was applied. The reference populations were all CPP patients in the relevant CPP and all cancer patients with relevant cancer type, respectively, in the period. The Spearman's rank correlation coefficient was computed between the age-adjusted proportion of CPP patients without the cancer diagnosis and the age-adjusted proportion of cancer patients included in CPP considering patients living in different hospital referral areas.

Results

A total of 89 691 CPP patients and 49 787 cancer patients were eligible for analyses. Among all CPP patients considered, 56.9% were without the cancer diagnosis. This proportion was stable over the three years (Table 1). The proportion of CPP patients without the cancer diagnosis

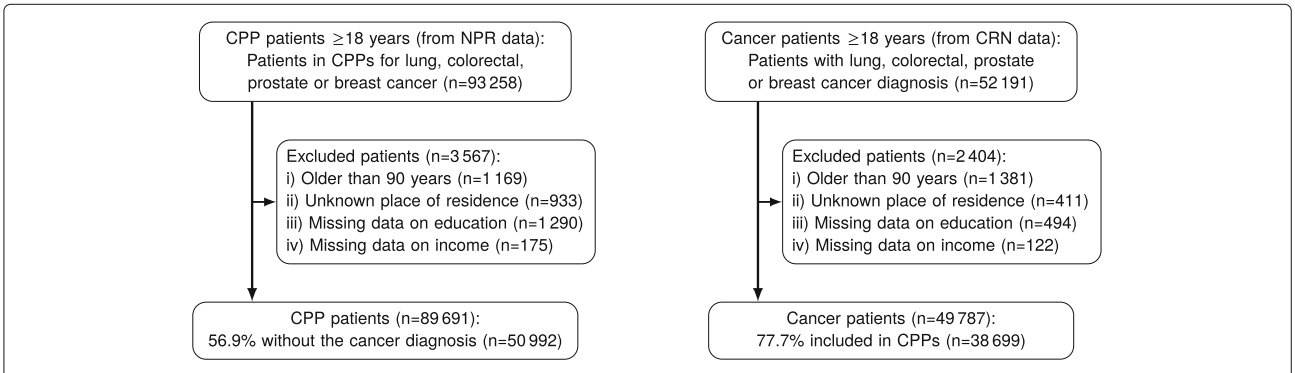

Fig. 1 Flowchart for CPP patients and cancer patients, Norway 2015-2017

Table 1 Characteristics of CPP patients and cancer patients. Norway, 2015-2017

	Lung		Colorectal		Prostate	Breast	Total
	Male	Female	Male	Female			
	CPP patients, n (% CPP patients without the cancer diagnosis)						
Patients	7 461 (46.3%)	6 428 (43.9%)	15 802 (64.6%)	16 824 (69.3%)	19 897 (48.7%)	23 279 (56.5%)	89 691 (56.9%)
Year							
2015	2 375 (47.2%)	2 055 (43.5%)	4 726 (63.0%)	5 109 (68.1%)	6 113 (51.1%)	7 487 (56.8%)	27 865 (56.9%)
2016	2 521 (45.8%)	2 143 (44.1%)	5 660 (65.6%)	5 935 (69.6%)	6 992 (47.6%)	7 785 (56.9%)	31 036 (57.0%)
2017	2 565 (45.9%)	2 230 (44.1%)	5 416 (65.0%)	5 780 (70.1%)	6 792 (47.6%)	8 007 (56.0%)	30 790 (56.7%)
Age group							
Under 50	344 (78.5%)	294 (70.4%)	1 546 (83.4%)	1 772 (84.8%)	389 (70.2%)	8 511 (79.3%)	12 856 (80.1%)
50-59	838 (60.3%)	789 (50.6%)	2 480 (74.4%)	2 493 (78.2%)	2 841 (59.0%)	5 106 (52.5%)	14 547 (62.2%)
60-69	2 251 (45.3%)	1 989 (42.7%)	4 240 (62.9%)	4 088 (70.9%)	8 533 (51.3%)	4 888 (39.0%)	25 989 (52.8%)
70-79	2 778 (40.8%)	2 372 (39.0%)	4 816 (59.4%)	5 080 (65.7%)	6 720 (42.6%)	3 216 (40.9%)	24 982 (49.8%)
80-90	1 250 (42.2%)	984 (44.7%)	2 720 (56.9%)	3 391 (58.1%)	1 414 (35.1%)	1 558 (32.6%)	11 317 (48.5%)
Income							
Low	1 567 (42.0%)	2 936 (41.9%)	2 573 (63.1%)	6 933 (66.0%)	2 208 (47.0%)	6 402 (52.6%)	22 619 (55.2%)
Medium	4 259 (44.6%)	2 838 (44.3%)	8 258 (63.4%)	7 563 (70.5%)	9 696 (46.1%)	11 117 (56.9%)	43 731 (56.1%)
High	1 635 (54.9%)	654 (51.1%)	4 971 (67.5%)	2 328 (75.2%)	7 993 (52.2%)	5 760 (60.3%)	23 341 (59.9%)
Education							
Low	2 641 (42.5%)	2 553 (41.7%)	4 209 (65.2%)	5 312 (67.8%)	3 889 (45.9%)	5 132 (55.9%)	23 736 (55.6%)
Medium	3 683 (46.6%)	2 947 (43.1%)	7 759 (64.1%)	7 603 (68.3%)	10 108 (47.9%)	9 707 (53.1%)	41 807 (55.3%)
High	1 137 (54.4%)	928 (52.5%)	3 834 (65.0%)	3 909 (73.3%)	5 900 (51.8%)	8 440 (60.9%)	24 148 (60.7%)
Comorbidity							
Low	5 118 (48.5%)	4 725 (45.7%)	13 020 (64.8%)	14 701 (69.7%)	17 868 (48.8%)	21 991 (56.9%)	77 423 (57.5%)
Medium	1 484 (41.9%)	1 235 (37.7%)	1 739 (62.8%)	1 403 (69.1%)	1 420 (46.8%)	833 (51.9%)	8 114 (52.3%)
High	859 (41.1%)	468 (41.7%)	1 043 (65.4%)	720 (61.4%)	609 (49.6%)	455 (49.2%)	4 154 (52.9%)
Travel time							
Short	5 695 (47.0%)	5 052 (44.5%)	12 384 (64.9%)	13 417 (69.7%)	15 535 (49.4%)	19 024 (56.5%)	71 107 (57.3%)
Medium	1 018 (44.5%)	820 (40.1%)	2 052 (63.4%)	2 044 (66.4%)	2 646 (45.8%)	2 726 (58.6%)	11 306 (55.3%)
Long	747 (43.8%)	556 (43.7%)	1 366 (63.7%)	1 363 (69.8%)	1 714 (46.9%)	1 529 (53.6%)	7 275 (55.2%)
Hospital referral area⋆							
Min†	32.4%	29.8%	42.5%	48.1%	28.9%	36.8%	45.4%
Max†	66.2%	61.3%	83.2%	84.0%	59.5%	73.1%	69.4%
SD	8.4%	7.7%	10.9%	10.0%	6.9%	9.2%	5.9%
EQ‡	2.0	2.1	2.0	1.7	2.1	2.0	1.5
	Cancer patients, n (% cancer patients included in CPP)						
Patients	5 076 (78.9%)	4 629 (77.9%)	6 836 (81.8%)	6 471 (79.8%)	15 864 (64.4%)	10 911 (92.7%)	49 787 (77.7%)
Year							
2015	1 650 (73.8%)	1 543 (73.0%)	2 252 (77.2%)	2 131 (75.5%)	5 136 (55.2%)	3 609 (89.3%)	16 321 (72.0%)
2016	1 682 (80.8%)	1 531 (78.8%)	2 307 (83.5%)	2 207 (81.8%)	5 378 (67.6%)	3 549 (94.5%)	16 654 (79.8%)
2017	1 744 (82.0%)	1 555 (82.0%)	2 277 (84.7%)	2 133 (82.1%)	5 350 (69.9%)	3 753 (94.3%)	16 812 (81.3%)

Table 1 Characteristics of CPP patients and cancer patients. Norway, 2015-2017 *(Continued)*

	Lung		Colorectal		Prostate	Breast	Total
	Male	Female	Male	Female			
Age group							
Under 50	87 (85.1%)	105 (84.8%)	366 (69.9%)	382 (70.4%)	160 (71.3%)	1 886 (93.2%)	2 986 (85.7%)
50-59	396 (84.1%)	461 (84.4%)	752 (84.6%)	674 (80.7%)	1 667 (69.2%)	2 613 (92.9%)	6 563 (83.5%)
60-69	1 503 (81.5%)	1 376 (82.6%)	1 860 (84.4%)	1 434 (82.8%)	5 939 (69.7%)	3 207 (92.9%)	15 319 (79.9%)
70-79	2 039 (80.9%)	1 821 (79.5%)	2 350 (83.4%)	2 110 (82.5%)	5 920 (65.5%)	2 063 (92.2%)	16 303 (77.1%)
80-90	1 051 (69.0%)	866 (63.2%)	1 508 (77.7%)	1 871 (76.1%)	2 178 (42.4%)	1 142 (91.9%)	8 616 (67.8%)
Income							
Low	1 257 (72.2%)	2 273 (74.7%)	1 204 (78.7%)	2 984 (79.0%)	2 047 (56.8%)	3 336 (91.0%)	13 101 (77.2%)
Medium	2 942 (80.2%)	1 985 (80.1%)	3 702 (81.8%)	2 777 (80.3%)	8 199 (63.8%)	5 136 (93.3%)	24 741 (77.7%)
High	877 (84.4%)	371 (86.3%)	1 930 (83.8%)	710 (81.4%)	5 618 (67.9%)	2 439 (93.8%)	11 945 (78.4%)
Education							
Low	1 965 (77.3%)	1 978 (75.2%)	1 827 (80.1%)	2 181 (78.3%)	3 446 (61.0%)	2 473 (91.5%)	13 870 (76.0%)
Medium	2 474 (79.6%)	2 109 (79.6%)	3 393 (82.2%)	2 987 (80.7%)	8 000 (65.8%)	4 916 (92.7%)	23 879 (78.2%)
High	637 (81.5%)	542 (81.5%)	1 616 (82.9%)	1 303 (80.2%)	4 418 (64.4%)	3 522 (93.6%)	12 038 (78.8%)
Comorbidity							
Low	3 243 (81.4%)	3 179 (80.7%)	5 519 (83.1%)	5 498 (81.0%)	13 813 (66.2%)	10 219 (92.8%)	41 471 (79.3%)
Medium	1 110 (77.7%)	1 009 (76.3%)	820 (78.9%)	584 (74.1%)	1 352 (55.9%)	434 (92.4%)	5 309 (72.9%)
High	723 (70.0%)	441 (61.9%)	497 (72.6%)	389 (71.5%)	699 (43.9%)	258 (89.5%)	3 007 (65.0%)
Travel time							
Short	3 850 (78.4%)	3 620 (77.5%)	5 351 (81.2%)	5 129 (79.3%)	12 291 (64.0%)	8 915 (92.8%)	39 156 (77.6%)
Medium	708 (79.9%)	603 (81.3%)	900 (83.6%)	842 (81.5%)	2 202 (65.1%)	1 217 (92.8%)	6 472 (78.1%)
Long	518 (81.3%)	406 (77.1%)	585 (84.8%)	500 (82.2%)	1 371 (66.2%)	779 (91.1%)	4 159 (78.4%)
Hospital referral area⋆							
Min†	69.0%	67.6%	69.4%	67.2%	44.8%	82.6%	72.7%
Max†	87.7%	86.8%	89.9%	88.1%	74.6%	98.4%	84.5%
SD	5.5%	5.9%	5.1%	4.8%	8.5%	3.6%	3.8%
EQ‡	1.3	1.3	1.3	1.3	1.7	1.2	1.2

† Min and Max are minimum and maximum proportions in the 21 hospital referral areas. ‡ EQ - Extremal quotient, EQ=Max/Min. ⋆ For details on the 21 hospital referral areas see Appendix B (Table B1)

ranged from 43.9% for females in lung CPP to 69.3% for females in colorectal CPP. The proportion of CPP patients without the cancer diagnosis varied between the hospital referral areas (Table 1 and Table B1), from 45.4% to 69.4% for all four CPPs combined, and the variation in the proportions between the hospital referral areas was about two-fold across the CPP groups.

In total 77.7% of the cancer patients were included in relevant CPPs, and the proportion increased from 72.0% in 2015 to 81.3% in 2017 (Table 1). The proportion of cancer patients included in CPP varied from 64.4% for prostate cancer to 92.7% for breast cancer, and between the hospital referral areas from 72.7% to 84.5% for all four types of cancer combined (Table 1 and Table B1) and more markedly across the cancer groups.

Relationships with age, income, education, comorbidity and hospital referral area

The main results from the multivariate logistic regression analysis are the effects after mutually adjusting for all the other independent variables, and adjustment for the independent variables according to the DAG methodology showed largely similar results.

Age group

The adjusted analyses for all CPP patients showed an inverse age gradient, indicating lower odds ratio of not receiving the cancer diagnosis with increasing age (Table 2). The only exceptions were the oldest patients (80-90 years) in CPP for lung cancer. An inverse age gradient was not consistently found in the adjusted analyses for

Table 2 Associations between age, income, education, comorbidity, travel time and hospital referral area and the odds ratios of not receiving the cancer diagnosis in CPP patients and the odds ratio of being included in CPP in cancer patients. Norway, 2015-2017. Analyses with mutual adjustment for all variables included

	Lung		Colorectal		Prostate	Breast
	Male	Female	Male	Female		
	CPP patients: odds ratio of not receiving the cancer diagnosis. OR (95% CI)					
Age group						
Under 50	4.19 (3.19-5.52)	2.89 (2.20-3.80)	2.91 (2.50-3.38)	2.29 (1.97-2.67)	2.18 (1.75-2.73)	5.97 (5.51-6.47)
50-59	1.79 (1.52-2.12)	1.31 (1.11-1.55)	1.67 (1.49-1.87)	1.47 (1.30-1.65)	1.36 (1.25-1.49)	1.76 (1.62-1.90)
60-69	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
70-79	0.88 (0.78-0.99)	0.87 (0.77-0.99)	0.86 (0.79-0.94)	0.81 (0.73-0.88)	0.71 (0.66-0.75)	1.03 (0.94-1.13)
80-90	0.97 (0.84-1.12)	1.13 (0.96-1.33)	0.78 (0.70-0.87)	0.59 (0.53-0.65)	0.50 (0.45-0.57)	0.69 (0.61-0.78)
p-value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Income						
Low	0.76 (0.65-0.90)	0.94 (0.77-1.14)	0.96 (0.85-1.07)	0.96 (0.85-1.09)	1.02 (0.92-1.13)	1.15 (1.05-1.26)
Medium	0.82 (0.72-0.93)	0.91 (0.76-1.10)	0.99 (0.91-1.08)	0.99 (0.89-1.12)	0.96 (0.90-1.03)	1.10 (1.02-1.18)
High	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
p-value[†]	0.001	0.803	0.493	0.444	0.828	0.003
Education						
Low	0.69 (0.60-0.81)	0.74 (0.62-0.88)	1.03 (0.93-1.14)	1.00 (0.89-1.11)	0.85 (0.78-0.93)	1.08 (0.99-1.17)
Medium	0.80 (0.69-0.92)	0.79 (0.67-0.92)	1.00 (0.92-1.09)	0.97 (0.88-1.07)	0.90 (0.84-0.96)	0.95 (0.89-1.02)
High	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
p-value[†]	<0.001	0.003	0.54	0.955	<0.001	0.146
Comorbidity						
Low	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Medium	0.90 (0.80-1.02)	0.79 (0.69-0.91)	1.10 (0.99-1.23)	1.14 (1.01-1.29)	1.05 (0.94-1.18)	1.29 (1.11-1.49)
High	0.90 (0.77-1.05)	0.95 (0.78-1.15)	1.20 (1.05-1.38)	0.92 (0.78-1.08)	1.25 (1.06-1.48)	1.35 (1.11-1.65)
p-value[†]	0.07	0.025	0.003	0.826	0.008	<0.001
Travel time						
Short	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Medium	1.03 (0.89-1.19)	0.92 (0.78-1.08)	1.01 (0.90-1.12)	0.93 (0.83-1.04)	0.94 (0.86-1.03)	1.13 (1.03-1.24)
Long	0.97 (0.80-1.16)	0.94 (0.76-1.16)	0.98 (0.86-1.12)	1.02 (0.89-1.18)	0.92 (0.82-1.04)	1.08 (0.95-1.23)
p-value[†]	0.876	0.353	0.825	0.718	0.09	0.026
Hospital referral area[‡]						
p-value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
	Cancer patients: odds ratio of being included in CPP. OR (95% CI)					
Age group						
Under 50	1.14 (0.61-2.10)	1.05 (0.60-1.85)	0.41 (0.32-0.54)	0.48 (0.37-0.63)	0.98 (0.69-1.39)	0.98 (0.78-1.24)
50-59	1.14 (0.84-1.55)	1.07 (0.80-1.43)	0.98 (0.77-1.24)	0.83 (0.65-1.05)	0.96 (0.85-1.08)	0.98 (0.80-1.20)
60-69	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
70-79	1.02 (0.85-1.21)	0.87 (0.73-1.05)	0.99 (0.83-1.17)	1.06 (0.89-1.28)	0.84 (0.78-0.92)	1.00 (0.81-1.25)
80-90	0.55 (0.46-0.67)	0.40 (0.33-0.49)	0.73 (0.61-0.88)	0.74 (0.62-0.89)	0.34 (0.31-0.38)	1.04 (0.80-1.35)
p-value	<.001	<.001	<.001	<.001	<.001	0.996

Table 2 Associations between age, income, education, comorbidity, travel time and hospital referral area and the odds ratios of not receiving the cancer diagnosis in CPP patients and the odds ratio of being included in CPP in cancer patients. Norway, 2015-2017. Analyses with mutual adjustment for all variables included *(Continued)*

	Lung		Colorectal		Prostate	Breast
	Male	Female	Male	Female		
Income						
Low	0.59 (0.46-0.75)	0.64 (0.45-0.90)	0.77 (0.62-0.96)	0.85 (0.67-1.09)	0.82 (0.72-0.92)	0.77 (0.60-0.98)
Medium	0.91 (0.73-1.14)	0.73 (0.53-1.02)	0.87 (0.73-1.02)	0.88 (0.71-1.11)	0.98 (0.90-1.06)	0.99 (0.80-1.22)
High	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
p-value†	<0.001	0.009	0.017	0.257	0.005	0.014
Education						
Low	0.93 (0.73-1.19)	0.97 (0.74-1.28)	0.87 (0.71-1.05)	0.91 (0.75-1.11)	1.03 (0.93-1.15)	0.84 (0.67-1.05)
Medium	0.92 (0.73-1.16)	1.04 (0.80-1.36)	0.94 (0.80-1.11)	0.99 (0.83-1.19)	1.12 (1.03-1.22)	0.95 (0.78-1.14)
High	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
p-value†	0.699	0.555	0.142	0.281	0.407	0.124
Comorbidity						
Low	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Medium	0.82 (0.69-0.98)	0.80 (0.67-0.96)	0.76 (0.63-0.91)	0.68 (0.55-0.83)	0.73 (0.65-0.82)	0.96 (0.67-1.40)
Much	0.58 (0.48-0.70)	0.41 (0.33-0.51)	0.56 (0.45-0.70)	0.61 (0.48-0.77)	0.50 (0.43-0.59)	0.72 (0.47-1.10)
p-value†	<0.001	<0.001	<0.001	<0.001	<0.001	0.165
Travel time						
Short	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Medium	1.09 (0.88-1.35)	1.19 (0.94-1.51)	0.96 (0.78-1.18)	0.98 (0.80-1.19)	1.06 (0.96-1.18)	1.11 (0.87-1.42)
Long	1.05 (0.80-1.37)	0.85 (0.64-1.13)	1.10 (0.85-1.43)	0.98 (0.75-1.28)	1.21 (1.06-1.39)	0.78 (0.59-1.04)
p-value†	0.535	0.774	0.652	0.815	0.006	0.295
Hospital referral area‡						
p-value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

† *P*-value for linear trend. ‡ OR estimates with 95% CI for the hospital referral areas are shown in Appendix B (Table B2)

the cancer patients (Table 2). However, the oldest patients (80-90 years) had lower odds ratio of being included in CPP for all cancer diagnoses except for breast cancer, along with the youngest colorectal cancer patients (under 50).

Income

A positive income gradient was found for male lung CPP patients, indicating increased odds ratio of not receiving the cancer diagnosis with increasing income. However, for breast CPP patients the opposite was true. For the cancer patients, a positive income gradient was found, indicating increased odds ratio of being included in CPP with increasing income, although the relationship was not statistically significant for female colorectal cancer patients.

Education

A positive education gradient was found for patients for lung CPP (male and female) and prostate CPP, indicating increased odds ratio of not receiving the cancer diagnosis with increasing level of education. For cancer patients no education gradient was found.

Comorbidity

A positive comorbidity gradient was found for patients in colorectal CPP (male), prostate CPP and breast CPP, suggesting increased odds ratio of not receiving the cancer diagnosis with increasing comorbidity. For cancer patients a clear negative comorbidity gradient was found for all cancer groups, except breast cancer patients, i.e., decreased odds ratio of being included in CPP with increasing comorbidity.

Travel time

No gradient for travel time was found for CPP patients. For cancer patients a positive gradient for travel time was found for patients with prostate cancer, the longer travel time to hospital, the higher the odds ratio of being included in CPP.

Hospital referral area

Substantial differences were found between the hospital referral areas both regarding the odds ratio of not receiving the cancer diagnosis among all the CPP patients and in the odds ratio of being included in a CPP among cancer patients (Table 2 and Table B2).

Relationships between the proportions

Correlation analysis comparing the age-adjusted proportions of CPP patients without the cancer diagnosis with the age-adjusted proportions of cancer patients included in CPP across the hospital referral areas did not show definite positive relations for any cancer site (Fig. 2).

Correlation analysis comparing the age-adjusted proportions of CPP patients without the cancer diagnosis in the 21 hospital referral areas across the six CPP groups showed some positive associations. Associations were found between the proportions for prostate CPP and colorectal (both male and female) CPP (Table B3). Also, comparing the age-adjusted proportion of cancer patients included in CPP in the 21 hospital referral areas across the six cancer groups showed some positive associations. Associations were found between the proportions for female colorectal cancer and lung (both male and female) cancer (Table B3). However, most correlation coefficients, except for those correlating proportions in men and women for the same cancer type, were relatively low. The overall impression is that neither the proportions of CPP patients without the cancer diagnosis nor the proportions of cancer patients included in CPP across the cancer groups are consistently ranked in the hospital referral areas (Fig. 3).

Discussion

This study, which includes complete CPP and cancer data for three years in Norway, showed that the patient's age and place of residence were the two most important factors for describing variation in proportions of CPP patients without the cancer diagnosis and proportions of cancer patients included in CPPs. The proportions varied substantially across the different types of CPPs and across the different cancer groups. As the probability of not receiving the cancer diagnosis for a patient in a CPP is related to both the risk of cancer and the probabilities of being included in a CPP for those with and without the cancer (See Appendix A. Conditional probabilities), the interpretations must account for these factors.

CPP guidelines

In general, the CPP guidelines ensure that all patients should have equal access to CPPs in Norway. The highest proportions of CPP patients without the cancer diagnosis were found in CPPs for colorectal cancer (65% and 69% for male and female, respectively) and breast cancer (57%). Less than 50% of the patients in CPPs for lung and prostate ended up without the cancer diagnosis. These

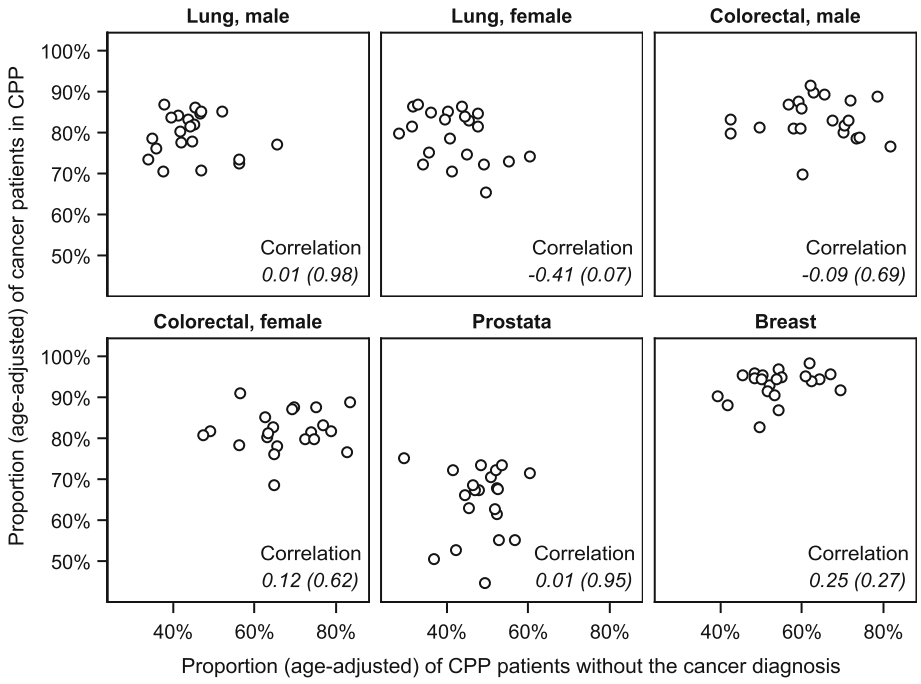

Fig. 2 Scatter plots for age-adjusted proportions of patients in CPP without the cancer diagnosis and age-adjusted proportions of cancer patients included in CPP in the 21 hospital referral areas. Spearman's correlation coefficients (*p*-value)

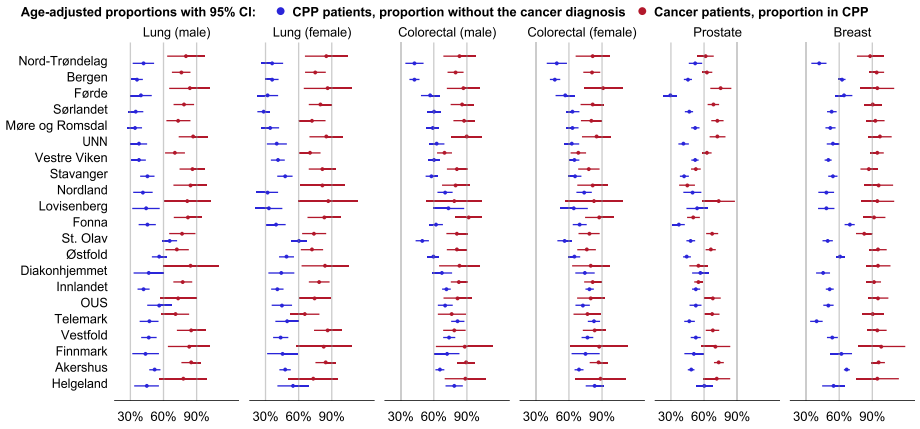

Fig. 3 Patients in CPP without the cancer diagnosis (blue) and cancer patients in CPP (red), age-adjusted proportions with 95% confidence intervals in the 21 hospital referral areas, ordered by the rank of the total proportion for CPP patients

differences may be explained by the "filter functions" for CPP for prostate and lung cancer. Only specialists in urology include patients to CPP for prostate cancer and the guidelines specify that patients should not be referred to CPP for prostate cancer when treatment is not appropriate due to age or comorbidity. Before inclusion in CPP for lung cancer, an X-ray image of the lungs is required in addition to respiratory symptoms. Similar filter functions are lacking for CPP for colorectal and breast cancer. The lowest proportion of cancer patients included in CPP was found for prostate cancer patients (64%).

Age and comorbidity

The highest proportion of CPP patients without the cancer diagnosis was found for the youngest patients and the proportion decreased with increasing age. The negative age gradient found in CPP patients without the cancer diagnosis might be explained by an increasing cancer incidence by age with lower probability for younger patients to have a cancer diagnosis. Given the same symptoms, an older patient is more likely to have cancer compared to a younger patient. A high proportion of CPP patients without the cancer diagnosis among the younger suggests that inclusion in CPPs in Norway follows the guidelines and is based on symptoms, signs and tests rather than the expected chance of detecting cancer.

Among cancer patients, except for breast cancer, the oldest patients had lower odds ratio of being included in a CPP than patients in the reference category, patients aged 60-69. This is in line with studies from Norway and Denmark [17, 22, 23]. One explanation might be that the elderly have higher comorbidity and more contact with the health care system. Cancer may be diagnosed during follow-up of other illnesses. The youngest colorectal cancer patients (under 50 years) also had lower odds ratio of being included in CPP, probably because the symptoms of younger colorectal cancer patients are less specific and harder to identify. Interestingly, more than 90% of the breast cancer patients were included in CPP, and no age differences were found. This high proportion and equality among the age groups are most likely due to the uniform structure and practice of breast diagnostic centres in Norway and the national breast screening programme for women aged 50 to 69. In all cancer patients, the probability of being included in CPP decreased with higher level of comorbidity, consistent with the findings of Nilssen et al. [17]. According to guidelines, patients with prostate cancer and high comorbidity or high age are not to be included in CPP if curative treatment is not relevant. Other patient groups may be considered similarly.

Income and education

The effects of income and education were not consistent across the CPP groups. In a report on social inequalities and cancer in Norway [24], associations between both income and education level and the risk of cancer were found. The risk of cancer increased with low level of income for males for lung and colorectal cancer, and increased risk of cancer with low level of education was found for lung cancer and among females for colorectal cancer. In contrast, increased risk of cancer with high levels of income and education was found for prostate and breast cancer. The observed differences in the odds ratio of not receiving the cancer diagnosis between the income groups for CPPs for lung (male) and breast cancer, in this study, might be due to different risks of cancer in the income groups between the CPPs.

The probability of being referred to a CPP, both for those with and without cancer, may also differ between income and education groups. Based on data in this study, only the probability for those with cancer can be estimated (Appendix A). The observed differences in income

and education gradients for CPP patients without the cancer diagnosis may diminish when the risk of cancer and the probabilities of being included in a CPP are taken into consideration. A systematic review concluded that women in Europe from more socioeconomically deprived areas were less likely to attend breast cancer screening [25]. Higher income and education groups might be more eager to be included in CPPs in order to assess their cancer symptoms. It is documented that patients from higher social classes communicate more actively with clinicians [26]. Therefore, based on the present data, it is not possible to state consistent differences in the proportions of CPP patients without the cancer diagnosis in different levels of income and education.

For the cancer patients, consistent differences were found. The proportion of cancer patients included in CPPs was highest in the patients with high income, which is in line with a recent Norwegian study [17]. Other studies have shown that patients' socioeconomic status is associated with an increased likelihood of access to cancer care [27, 28]. However, in accordance with results of Nilssen et al. [17], we found no such effect of education for any of the cancer groups.

Place of residence

Substantial variation between the hospital referral areas was found, both for the proportion of CPP patients without the cancer diagnosis and the proportion of cancer patients included in CPP. The proportions in neighbouring hospital referral areas were not more similar than for more distant hospital referral areas. The observed variation between the hospital referral areas is probably related to both differences in clinical practice and differences in capacity. Unwarranted variation in health care is mainly due to services that can be defined as preference-sensitive or supply-sensitive [29]. Preference-sensitive care represents clinical practice, references and beliefs of a single clinician or department rather than a clear evidence-based approach. Supply-sensitive care refers to local capacity of health care resources, such as out-patients clinics and diagnostic work-ups. In addition, the hospital trusts have public funding contracts with private specialists in order to secure sufficient capacity, and different utilisation of private specialists among the health care trusts may contribute to the observed variation. Additionally, hospitals may have included patients in CPPs at somewhat different points in the diagnostic and staging process, although clear guidelines exist. This may also affect the observed variation.

One might expect that a hospital referral area with a high proportion of patients without the cancer diagnosis in CPPs, also has a high proportion of diagnosed cancer patients included in CPPs. However, such associations were not found, suggesting that a wide funnel into CPPs does not necessarily lead to higher proportions of cancer patients included in CPPs. This finding is in line with a study from England on variation in referral threshold and variation in the accurate selection of patients in fast-track referrals from GPs for possible cancer [30]. It was found that widening the funnel did not increase the proportion of cancer patients included in CPP. However, it did result in a large increase in demand for diagnostic services with a possible risk of over-diagnosis and over-treatment. Therefore, tools that focus on increasing diagnostic accuracy are probably more effective than applying wider funnels to increase the proportion of cancer patients included in CPPs. A Nordic initiative for prostate cancer can serve as an example: application of a new blood-based test in addition to PSA resulted in promising results for a more accurate selection of patients into CPP for prostate cancer [31–33].

It was not consistently the same hospital referral areas that had the highest or lowest proportions of CPP patients without the cancer diagnosis or the highest or lowest proportions of cancer patients included in CPP. As the diagnostic work-ups for the different CPPs are done at different departments/units in the hospitals, it is reasonable to see varying degrees of inclusion to CPP in the hospital referral areas across the different CPPs. A hospital might have lower threshold for including patients in CPP in some areas due to capacity or clinical practice (for example, the gastroenterological and lung clinics) while having higher threshold for other areas due to capacity constraints or stricter clinical practice (for example, prostate cancer).

Experiences with CPPs

CPPs in Norway were introduced as a joint action from health politicians, health bureaucrats and clinicians as an initiative from the Ministry of Health and patient organisations. The experiences with CPPs in Norway are so far positive [34, 35]. In Norway, decreased waiting times have been observed before and during implementation of CPPs [36]. Studies from Denmark [3, 37] and Sweden [38] have documented reduced waiting times, and a study from Denmark showed increased survival among patients in CPP compared to patients not in CPP for some cancer sites [23]. It is worth noting that Denmark started CPP eight years before Norway, a period in which cancer care made great progress in Norway.

CPPs may also have some unintended consequences. Wilkens et al. discuss challenges with possible crowding-out effects as a result of implementing CPP [5]. A Norwegian study, with interviews of physicians and patients, indicated possible crowding-out effects as a result of the standardised target times in CPPs [35, 39]. In a qualitative study on CPP in Sweden, implementation of CPPs was accompanied by unintended effects such as longer

waiting times for other patients and patient groups in need of the same health care resources [40]. However, in Norway these types of crowding-out effects are not observed in quantitative data, such as national data for waiting times [41].

Strengths and limitations

The strength of this study is the use of individualised data for the complete Norwegian population of CPP patients and cancer patients for three years. The completeness of data eliminates selection bias. However, there are some limitations.

Firstly, the proportions studied empirically in this paper reflect two underlying conditional probabilities, the probability of not having cancer given that an individual is assigned to a CPP, and the probability of being included in a CPP given that the patient is diagnosed with cancer. The probability of not having cancer for an individual included in a CPP can be expressed in terms of the overall probability of cancer and the ratio of the probabilities of being assigned to a CPP for those with and without cancer (Appendix A). However, it is not possible to estimate all relevant terms involved with the data available in the current study. Such analysis requires data on the entire Norwegian population, including those not in contact with the hospitals. It is important to note that the relationships presented in Appendix A and discussed above do not invalidate the findings as presented; the relationships reflect the associations as they are in Norwegian cancer care. The explanations for the findings are not, however, self-evident and may be open for discussion.

Secondly, it was not possible in this study to evaluate at which point in the diagnostic and staging work-up patients are included in CPPs. The possibility that cancer patients have been retrospectively included in CPPs cannot be ruled out. However, this probably contributes only to a small degree to the observed geographic variation.

Thirdly, the presented results are mutually adjusted for all the predictors, i.e., there is a risk of Table II fallacy. However, adjusting the predictors according to a DAG framework basically reproduced the results in Table 2.

Conclusion

Among the CPP patients, the youngest patients had the highest probability of not receiving the cancer diagnosis, and among the cancer patients the oldest patients had the lowest probability of being included in a CPP. This is most likely due to increasing risk of cancer and increasing contacts with the health care system with age. The lack of consistent differences among CPP patients according to income, education, comorbidity and travel time to hospital with regard to the proportion not diagnosed with cancer is encouraging and suggests that CPP as a health service in Norway is equitably distributed. Increasing diagnostic accuracy is probably a more effective way to increase the proportions of cancer patients included in CPPs, as lowering the threshold for referring patients into CPPs did not have an effect. Lowering the threshold may also lead to an increase in demand for diagnostic services with a possible risk of over-diagnosis, over-treatment and crowding-out effects for other patients. Unwarranted variation according to patients' place of residence was documented, both for CPP patients without the cancer diagnosis and for cancer patients included in CPP. This variation is probably related to both differences in clinical practice and capacity at the Norwegian hospitals and should be further investigated.

Abbreviations

CCI: Charlson comorbidity index; CPP: Cancer patient pathways; CRN: Cancer Registry of Norway; DAG: Directed acyclic graph GP: General practitioner; ICD-10: International Statistical Classification of Diseases and Related Health Problems diagnosis codes; ISCED: International standard classification of education; NPR: Norwegian Patient Registry; SES: Socioeconomic status; SSB: Statistics Norway

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12913-021-07250-1.

Additional file 1: Appendix

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Authors' contributions

F.O., L.B. and K.M.T. conceived and designed the study. F.O. facilitated and analysed the data. F.O., B.K.J. and I.H. contributed to the analytical strategy. F.O., L.B. and B.K.J. drafted the manuscript. All authors participated in the revision of the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

The original data were not collected by the authors but made available by record-linkage, using the unique 11 digits personal ID, between the Norwegian Patient Registry (NPR), Cancer Registry of Norway (CRN) and the Statistics Norway (SSB) (NPR ref. 18/28584-13, CRN ref. 18/265 DU-3294 and SSB ref. W19/0477). Individual-level health data are, by definition, considered to be sensitive information in the Norwegian legislation, even if de-identified and strict confidentiality requirements prevent sharing of data in public repositories. According to a contract signed with the NPR, CRN and the SSB, the project is not allowed to forward data, or subsets of data, to other researchers, except project members named in the Data Protection Impact Assessment (DPIA). Furthermore, we are required to delete the linked data set by 31 December 2023. However, any researcher with approval of an exemption from professional secrecy requirements for the use of personal health data in research from the Regional Committee for Medical and Health Research Ethics (REK) would be able to create an almost identical (updated) dataset by applying to the NPR, the CRN and the SSB.

Declarations

Ethics approval and consent to participate

The study is based on secondary use of clinical administrative data. For this reason, approval from Regional Committees for Medical and Health Research Ethics (REK) is not required, but REK has given exemption from the duty of confidentiality (ref. 20627/REK sør-øst A). The project has conducted a Data Protection Impact Assessment (DPIA). Public access to this type of data is closed. Access was given by applying to the NPR, the CRN and the SSB. According to Norwegian law, further ethical approval or obtaining informed consent was not required for this study. All methods were performed in accordance with the relevant guidelines and regulations.

Consent for publication

Not required.

Competing interests

None declared.

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Publisher's Note

Appendix

A. Conditional probabilities

Consider what happens during the study period to an individual selected at random from a subgroup in the population. Let "Cancer" represent the event that the individual actually has cancer of a particular type, and let "CPP" represent the event that the individual is referred to the corresponding cancer patient pathway.

The probability of not having this type of cancer, conditional on the individual being referred to the corresponding CPP, can be expressed as

$$P(\overline{\text{Cancer}}|\text{CPP}) = \frac{P(\text{CPP and } \overline{\text{Cancer}})}{P(\text{CPP})}$$

Applying Bayes' theorem

$$P(\overline{\text{Cancer}}|\text{CPP}) = \frac{P(\text{CPP}|\overline{\text{Cancer}})P(\overline{\text{Cancer}})}{P(\text{CPP}|\text{Cancer})P(\text{Cancer}) + P(\text{CPP}|\overline{\text{Cancer}})P(\overline{\text{Cancer}})}$$

Dividing both numerator and denominator with $P(\text{CPP}|\overline{\text{Cancer}})$

$$P(\overline{\text{Cancer}}|\text{CPP}) = \frac{P(\overline{\text{Cancer}})}{\frac{P(\text{CPP}|\text{Cancer})}{P(\text{CPP}|\overline{\text{Cancer}})}P(\text{Cancer}) + P(\overline{\text{Cancer}})}$$

Finally, dividing both numerator and denominator with $P(\overline{\text{Cancer}})$, the probability of not having this type of cancer, conditional on the individual being referred to the corresponding CPP, can be written as

$$P(\overline{\text{Cancer}}|\text{CPP}) = \frac{1}{\frac{P(\text{CPP}|\text{Cancer})}{P(\text{CPP}|\overline{\text{Cancer}})}\frac{P(\text{Cancer})}{P(\overline{\text{Cancer}})} + 1}$$

This equation expresses the first conditional probability of interest, the probability of not having cancer conditional on the individual being referred to the corresponding CPP; $P(\overline{\text{Cancer}}|\text{CPP})$, in terms of the second one, the probability of being referred to CPP conditional on the individual having the corresponding cancer; $P(\text{CPP}|\text{Cancer})$. But the expression also involves the overall probability of having the cancer in question; $P(\text{Cancer})$, and the conditional probability of being referred to the CPP for someone without the cancer; $P(\text{CPP}|\overline{\text{Cancer}})$.

This study is based on data on all Norwegian patients in CPPs and all Norwegian patients with a cancer diagnosis. It is not possible to make statements about associations with the overall probability of having cancer or the probability of being referred to a

CPP for a person without cancer. That would require data on the entire Norwegian population. Thus, despite the mathematical relationship described above, it is still relevant to examine associations with both proportions by a statistical approach, as carried out in this work.

A wide funnel into a CPP will in general correspond to large values of both probabilities $P(\text{CPP}|\text{Cancer})$ and $P(\text{CPP}|\overline{\text{Cancer}})$. The expression above shows that the ratio between these probabilities is essential. In fact, the probability of not having cancer for someone referred to a CPP is a decreasing function of this ratio. Studying associations between the proportion of CPP patients without cancer and other factors is for this reason largely the same as comparing the width of the funnel into CPP for cancer and non-cancer patients. However, the proportion is also a decreasing function of the basic probability of cancer, so results may in addition reflect associations with cancer incidence rates.

B. Supplementary tables and figures

Table B1: CPP patients and cancer patients, by hospital referral area. Norway, 2015-2017.

	Lung		Colorectal		Prostate	Breast	Total
	Male	Female	Male	Female			
CPP patients, n (% CPP patients diagnosed without cancer)							
Number of patients	7 461 (46.3%)	6 428 (43.9%)	15 802 (64.6%)	16 824 (69.3%)	19 897 (48.7%)	23 279 (56.5%)	89 691 (56.9%)
Hospital referral area							
Finnmark	158 (43.7%)	135 (46.7%)	264 (73.5%)	254 (78.0%)	291 (51.2%)	307 (58.6%)	1 409 (60.5%)
UNN	306 (37.3%)	247 (38.9%)	573 (62.8%)	565 (63.0%)	741 (41.8%)	826 (50.8%)	3 258 (50.8%)
Nordland	247 (42.1%)	160 (31.3%)	623 (70.0%)	638 (74.6%)	315 (48.9%)	475 (45.7%)	2 458 (58.5%)
Helgeland	136 (54.4%)	132 (54.5%)	536 (79.7%)	555 (83.4%)	422 (59.5%)	291 (51.9%)	2 072 (69.4%)
Nord-Trøndelag	196 (44.9%)	169 (36.7%)	293 (43.0%)	270 (51.1%)	621 (51.0%)	423 (38.8%)	1 972 (45.4%)
St. Olav	568 (66.2%)	517 (61.3%)	610 (48.9%)	614 (54.4%)	1 200 (48.8%)	993 (47.8%)	4 502 (53.0%)
Møre-Romsdal	322 (35.7%)	238 (33.6%)	859 (57.6%)	851 (61.8%)	1 460 (53.0%)	1 082 (49.8%)	4 812 (52.6%)
Førde	182 (40.1%)	134 (37.3%)	358 (56.4%)	343 (58.0%)	367 (28.9%)	527 (61.7%)	1 911 (50.0%)
Bergen	533 (35.6%)	418 (35.2%)	866 (42.5%)	904 (48.1%)	1 359 (45.3%)	2 257 (63.9%)	6 337 (50.4%)
Fonna	341 (46.0%)	230 (41.7%)	674 (61.9%)	724 (69.3%)	495 (36.4%)	1 342 (73.1%)	3 806 (61.3%)
Stavanger	486 (46.1%)	430 (47.9%)	804 (59.0%)	810 (64.9%)	1 024 (43.1%)	1 239 (55.7%)	4 793 (53.4%)
Østfold	539 (56.4%)	450 (49.1%)	876 (59.0%)	943 (64.1%)	1 447 (43.8%)	1 659 (61.9%)	5 914 (55.9%)
Akershus	805 (53.2%)	722 (48.8%)	1 578 (66.3%)	1 666 (70.4%)	2 079 (48.5%)	3 493 (69.8%)	10 343 (62.3%)
OUS	226 (55.8%)	238 (44.1%)	657 (70.6%)	723 (73.4%)	725 (52.7%)	973 (49.7%)	3 542 (59.1%)
Lovisenberg	141 (48.2%)	95 (42.1%)	224 (72.3%)	213 (67.6%)	269 (54.3%)	396 (52.5%)	1 338 (57.4%)
Diakonhjemmet	121 (51.2%)	142 (46.5%)	370 (68.4%)	438 (73.1%)	432 (56.7%)	554 (43.7%)	2 057 (57.8%)
Innlandet	582 (42.1%)	535 (41.5%)	1 842 (71.9%)	2 155 (79.4%)	1 592 (53.8%)	1 646 (50.2%)	8 352 (62.1%)
Vestre Viken	451 (37.0%)	455 (40.4%)	1 117 (60.6%)	1 166 (64.9%)	1 895 (51.1%)	1 989 (49.3%)	7 073 (52.8%)
Vestfold	402 (48.5%)	385 (44.4%)	1 005 (74.2%)	1 140 (76.5%)	1 050 (52.2%)	1 053 (51.9%)	5 035 (61.1%)
Telemark	278 (47.8%)	234 (48.3%)	985 (83.2%)	1 091 (84.0%)	799 (48.4%)	590 (36.8%)	3 977 (65.0%)
Sørlandet	441 (32.4%)	362 (29.8%)	688 (58.6%)	761 (62.7%)	1 314 (47.7%)	1 164 (52.1%)	4 730 (50.0%)
Cancer patients, n (% cancer patients included in CPP)							
Number of patients	5 076 (78.9%)	4 629 (77.9%)	6 836 (81.8%)	6 471 (79.8%)	15 864 (64.4%)	10 911 (92.7%)	49 787 (77.7%)
Hospital referral area							
Finnmark	104 (85.6%)	89 (80.9%)	83 (84.3%)	64 (87.5%)	196 (71.9%)	129 (98.4%)	665 (83.5%)
UNN	219 (87.7%)	174 (86.8%)	245 (86.9%)	251 (83.3%)	597 (72.2%)	420 (96.7%)	1 906 (84.1%)
Nordland	174 (82.2%)	137 (80.3%)	233 (80.3%)	198 (81.8%)	359 (44.8%)	269 (95.9%)	1 370 (74.5%)
Helgeland	80 (77.5%)	88 (68.2%)	126 (86.5%)	110 (83.6%)	243 (70.4%)	149 (94.0%)	796 (79.6%)
Nord-Trøndelag	135 (80.0%)	129 (82.9%)	203 (82.3%)	162 (81.5%)	495 (61.4%)	290 (89.3%)	1 414 (76.2%)
St. Olav	252 (76.2%)	269 (74.3%)	386 (80.8%)	355 (78.9%)	918 (67.0%)	626 (82.6%)	2 806 (75.4%)
Møre-Romsdal	280 (73.9%)	214 (73.8%)	415 (87.7%)	407 (79.9%)	940 (72.9%)	587 (92.5%)	2 843 (80.3%)
Førde	129 (84.5%)	102 (82.4%)	176 (88.6%)	164 (87.8%)	350 (74.6%)	213 (94.8%)	1 134 (84.3%)
Bergen	445 (77.1%)	362 (74.9%)	625 (79.7%)	581 (80.6%)	1 181 (63.0%)	865 (94.2%)	4 059 (77.3%)
Fonna	224 (82.1%)	161 (83.2%)	286 (89.9%)	252 (88.1%)	619 (50.9%)	387 (93.3%)	1 929 (76.4%)
Stavanger	301 (87.0%)	268 (83.6%)	416 (79.3%)	363 (78.2%)	1 096 (53.2%)	628 (87.4%)	3 072 (72.7%)
Østfold	330 (71.2%)	321 (71.3%)	445 (80.7%)	447 (75.8%)	1 237 (65.7%)	665 (95.0%)	3 445 (75.7%)
Akershus	441 (85.5%)	438 (84.5%)	603 (88.2%)	574 (85.9%)	1 450 (73.9%)	1 102 (95.6%)	4 608 (84.5%)
OUS	136 (73.5%)	173 (76.9%)	233 (82.8%)	245 (78.4%)	511 (67.1%)	512 (95.5%)	1 810 (80.1%)
Lovisenberg	87 (83.9%)	65 (84.6%)	82 (75.6%)	84 (82.1%)	173 (71.1%)	202 (93.6%)	693 (82.4%)
Diakonhjemmet	72 (81.9%)	92 (82.6%)	143 (81.8%)	151 (78.1%)	345 (54.2%)	327 (95.4%)	1 130 (76.9%)
Innlandet	437 (77.1%)	399 (78.7%)	626 (82.6%)	547 (81.2%)	1 344 (54.7%)	897 (91.3%)	4 250 (74.5%)
Vestre Viken	413 (69.0%)	393 (69.0%)	634 (69.4%)	609 (67.2%)	1 471 (63.0%)	1 070 (94.2%)	4 590 (72.7%)
Vestfold	244 (84.8%)	254 (84.3%)	329 (79.0%)	328 (81.7%)	753 (66.7%)	538 (94.2%)	2 446 (80.0%)
Telemark	198 (73.2%)	179 (67.6%)	218 (75.2%)	232 (75.4%)	599 (68.9%)	415 (89.9%)	1 841 (75.6%)
Sørlandet	375 (79.5%)	322 (78.9%)	329 (86.6%)	347 (81.8%)	987 (69.6%)	620 (89.8%)	2 980 (79.4%)

Table B2: Associations between hospital referral area and the odds ratios of being diagnosed without cancer among CPP patients and the odds ratio for being included in CPP among cancer patients. Norway, 2015-2017. Analyses with mutual adjustment for all variables included; age, income, education, comorbidity, travel time and hospital referral area.

	Lung		Colorectal		Prostate	Breast
	Male	Female	Male	Female		
	CPP patients: odds ratio of being diagnosed without cancer OR (95% CI)					
Hospital referral area						
Finnmark	0.70 (0.48-1.02)	0.92 (0.62-1.38)	1.41 (1.04-1.92)	1.44 (1.03-2.01)	1.20 (0.92-1.56)	0.70 (0.53-0.92)
UNN	0.57 (0.43-0.76)	0.68 (0.50-0.93)	0.88 (0.71-1.08)	0.74 (0.60-0.92)	0.79 (0.66-0.94)	0.50 (0.43-0.60)
Nordland	0.65 (0.48-0.88)	0.48 (0.33-0.69)	1.22 (0.99-1.50)	1.27 (1.02-1.57)	1.05 (0.83-1.34)	0.39 (0.31-0.48)
Helgeland	1.08 (0.74-1.57)	1.29 (0.89-1.89)	1.99 (1.57-2.53)	2.24 (1.74-2.88)	1.74 (1.40-2.15)	0.45 (0.35-0.59)
Nord-Trøndelag	0.76 (0.55-1.05)	0.61 (0.43-0.87)	0.40 (0.31-0.52)	0.49 (0.38-0.64)	1.17 (0.98-1.41)	0.30 (0.24-0.38)
St. Olav	1.70 (1.35-2.13)	1.58 (1.25-2.01)	0.51 (0.42-0.62)	0.54 (0.44-0.66)	1.02 (0.88-1.18)	0.42 (0.36-0.49)
Møre og Romsdal	0.51 (0.39-0.67)	0.52 (0.38-0.71)	0.72 (0.61-0.86)	0.75 (0.62-0.89)	1.19 (1.04-1.37)	0.48 (0.41-0.55)
Førde	0.56 (0.40-0.79)	0.62 (0.42-0.92)	0.67 (0.53-0.85)	0.65 (0.51-0.84)	0.46 (0.36-0.58)	0.76 (0.62-0.93)
Bergen	0.48 (0.38-0.61)	0.56 (0.44-0.73)	0.38 (0.32-0.45)	0.41 (0.34-0.48)	0.87 (0.76-1.00)	0.80 (0.71-0.90)
Fonna	0.73 (0.56-0.95)	0.74 (0.54-1.00)	0.84 (0.69-1.02)	1.04 (0.85-1.26)	0.62 (0.51-0.76)	1.11 (0.96-1.29)
Stavanger	0.69 (0.54-0.86)	0.93 (0.73-1.19)	0.73 (0.61-0.88)	0.84 (0.70-1.01)	0.79 (0.68-0.92)	0.54 (0.47-0.62)
Østfold	1.18 (0.95-1.48)	1.02 (0.81-1.30)	0.77 (0.65-0.92)	0.82 (0.69-0.97)	0.86 (0.75-0.98)	0.71 (0.62-0.81)
Akershus	1.00	1.00	1.00	1.00	1.00	1.00
OUS	1.02 (0.75-1.39)	0.78 (0.58-1.06)	1.18 (0.96-1.44)	1.20 (0.98-1.47)	1.18 (0.99-1.40)	0.45 (0.39-0.53)
Lovisenberg	0.71 (0.49-1.03)	0.64 (0.41-1.00)	1.15 (0.84-1.58)	0.74 (0.54-1.01)	1.18 (0.91-1.53)	0.43 (0.35-0.55)
Diakonhjemmet	0.78 (0.53-1.16)	0.80 (0.56-1.17)	1.15 (0.90-1.48)	1.23 (0.97-1.57)	1.39 (1.13-1.72)	0.42 (0.34-0.51)
Innlandet	0.69 (0.55-0.86)	0.77 (0.61-0.97)	1.32 (1.14-1.53)	1.71 (1.47-1.99)	1.21 (1.06-1.38)	0.45 (0.39-0.51)
Vestre Viken	0.51 (0.40-0.65)	0.68 (0.53-0.86)	0.79 (0.67-0.93)	0.82 (0.69-0.96)	1.10 (0.97-1.25)	0.44 (0.39-0.50)
Vestfold	0.81 (0.64-1.04)	0.83 (0.64-1.06)	1.51 (1.26-1.80)	1.48 (1.24-1.77)	1.16 (1.00-1.35)	0.53 (0.46-0.62)
Telemark	0.79 (0.60-1.05)	0.95 (0.70-1.28)	2.40 (1.96-2.93)	2.21 (1.82-2.69)	0.97 (0.82-1.14)	0.26 (0.22-0.32)
Sørlandet	0.44 (0.34-0.56)	0.44 (0.33-0.57)	0.77 (0.64-0.92)	0.78 (0.65-0.94)	0.93 (0.81-1.07)	0.51 (0.44-0.59)
p-value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
	Cancer patients: odds ratio of being included in CPP OR (95% CI)					
Hospital referral area						
Finnmark	1.01 (0.53-1.91)	0.91 (0.48-1.72)	0.66 (0.34-1.28)	1.21 (0.54-2.70)	0.79 (0.55-1.13)	3.61 (0.85-15.31)
UNN	1.34 (0.81-2.22)	1.32 (0.78-2.25)	0.83 (0.53-1.32)	0.88 (0.58-1.34)	0.85 (0.68-1.06)	1.49 (0.81-2.74)
Nordland	0.85 (0.52-1.39)	0.85 (0.51-1.43)	0.53 (0.35-0.80)	0.75 (0.48-1.17)	0.27 (0.21-0.34)	1.19 (0.60-2.34)
Helgeland	0.60 (0.33-1.10)	0.42 (0.24-0.72)	0.88 (0.49-1.56)	0.90 (0.51-1.59)	0.89 (0.65-1.21)	0.78 (0.37-1.63)
Nord-Trøndelag	0.70 (0.42-1.17)	1.00 (0.58-1.72)	0.59 (0.38-0.93)	0.71 (0.45-1.14)	0.55 (0.44-0.69)	0.41 (0.25-0.65)
St. Olav	0.55 (0.37-0.82)	0.56 (0.38-0.83)	0.54 (0.38-0.77)	0.64 (0.45-0.91)	0.68 (0.56-0.82)	0.23 (0.16-0.33)
Møre og Romsdal	0.48 (0.33-0.71)	0.55 (0.36-0.83)	0.91 (0.62-1.35)	0.68 (0.48-0.96)	0.90 (0.74-1.09)	0.61 (0.40-0.93)
Førde	0.91 (0.52-1.60)	0.80 (0.44-1.45)	1.02 (0.60-1.75)	1.20 (0.70-2.06)	1.01 (0.76-1.33)	0.87 (0.44-1.72)
Bergen	0.58 (0.41-0.82)	0.59 (0.41-0.85)	0.51 (0.37-0.70)	0.69 (0.51-0.95)	0.60 (0.51-0.72)	0.78 (0.52-1.17)
Fonna	0.80 (0.51-1.23)	0.95 (0.57-1.56)	1.18 (0.74-1.87)	1.23 (0.79-1.94)	0.34 (0.28-0.42)	0.68 (0.41-1.11)
Stavanger	1.13 (0.73-1.74)	1.00 (0.65-1.52)	0.49 (0.35-0.69)	0.61 (0.43-0.86)	0.36 (0.31-0.43)	0.33 (0.23-0.48)
Østfold	0.41 (0.29-0.59)	0.46 (0.32-0.66)	0.53 (0.38-0.75)	0.53 (0.38-0.73)	0.67 (0.56-0.79)	0.92 (0.58-1.45)
Akershus	1.00	1.00	1.00	1.00	1.00	1.00
OUS	0.50 (0.31-0.80)	0.62 (0.40-0.98)	0.65 (0.42-0.99)	0.59 (0.40-0.87)	0.76 (0.60-0.95)	0.97 (0.58-1.61)
Lovisenberg	0.89 (0.47-1.69)	1.04 (0.50-2.17)	0.41 (0.23-0.73)	0.79 (0.43-1.46)	0.81 (0.57-1.16)	0.68 (0.36-1.27)
Diakonhjemmet	0.75 (0.38-1.47)	0.81 (0.44-1.50)	0.53 (0.32-0.88)	0.58 (0.36-0.91)	0.43 (0.34-0.56)	0.92 (0.51-1.67)
Innlandet	0.59 (0.42-0.84)	0.68 (0.47-0.98)	0.63 (0.45-0.87)	0.73 (0.53-1.01)	0.41 (0.35-0.49)	0.52 (0.36-0.75)
Vestre Viken	0.36 (0.26-0.51)	0.40 (0.28-0.56)	0.28 (0.21-0.39)	0.34 (0.26-0.46)	0.60 (0.51-0.71)	0.76 (0.51-1.11)
Vestfold	0.98 (0.63-1.53)	1.03 (0.67-1.60)	0.49 (0.34-0.70)	0.76 (0.52-1.09)	0.75 (0.61-0.91)	0.79 (0.50-1.26)
Telemark	0.45 (0.29-0.68)	0.37 (0.24-0.56)	0.39 (0.26-0.58)	0.52 (0.35-0.76)	0.75 (0.61-0.93)	0.43 (0.28-0.66)
Sørlandet	0.67 (0.46-0.97)	0.66 (0.45-0.96)	0.84 (0.56-1.26)	0.75 (0.52-1.08)	0.78 (0.65-0.94)	0.43 (0.29-0.63)
p-value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

Table B3: Comparison of the age-adjusted proportions of CCP patients diagnosed without cancer across the six CPP groups, and comparison of the age-adjusted proportion of cancer patients included in CPP across the six cancer groups, in the 21 hospital referral areas. Spearman's correlation coefficients (p-value).

	Lung		Colorectal		Prostate	Breast
	Male	Female	Male	Female		
	CPP patients, proportion diagnosed without cancer, ρ_s (p-value)					
Lung, Male	1.00	0.77 (<0.01)	0.30 (0.18)	0.40 (0.07)	0.12 (0.61)	-0.07 (0.76)
Lung, Female		1.00	0.26 (0.25)	0.42 (0.06)	0.13 (0.59)	0.02 (0.92)
Colorectal, Male			1.00	0.86 (<0.01)	0.53 (0.01)	-0.19 (0.41)
Colorectal, Female				1.00	0.45 (0.04)	-0.09 (0.70)
Prostate					1.00	-0.50 (0.02)
Breast						1.00
	Cancer patients, proportion included in CPP, ρ_s (p-value)					
Lung, Male	1.00	0.81 (<0.01)	0.41 (0.06)	0.55 (<0.01)	0.09 (0.69)	0.30 (0.19)
Lung, Female		1.00	0.29 (0.21)	0.65 (<0.01)	0.25 (0.27)	0.23 (0.31)
Colorectal, Male			1.00	0.65 (<0.01)	0.32 (0.16)	0.25 (0.28)
Colorectal, Female				1.00	0.42 (0.06)	0.34 (0.14)
Prostate					1.00	0.34 (0.13)
Breast						1.00

Paper III

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Socioeconomic and geographic differences in ablation of atrial fibrillation in Norway - a national cohort study

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Abstract

Background: The aim of this study was to analyse whether there are patient related or geographic differences in the use of catheter ablation among atrial fibrillation patients in Norway.

Methods: National population-based data on individual level of all Norwegians aged 25 to 75 diagnosed with atrial fibrillation from 2008 to 2017 were used to study the proportion treated with catheter ablation. Survival analysis, by Cox regression with attained age as time scale, separately by gender, was applied to examine the associations between ablation probability and educational level, income level, place of residence, and follow-up time.

Results: Substantial socioeconomic and geographic variation was documented. Atrial fibrillation patients with high level of education and high income were more frequently treated with ablation, and the education effect increased with increasing age. Patients living in the referral area of St. Olavs Hospital Trust had around three times as high ablation rates as patients living in the referral area of Finnmark Hospital Trust.

Conclusions: Differences in health literacy, patient preference and demands are probably important causes of socioeconomic variation, and studies on how socioeconomic status influences the choice of treatment are warranted. Some of the geographic variation may reflect differences in ablation capacity. However, geographic variation related to differences in clinical practice and provider preferences implies a need for clearer guidelines, both at the specialist level and at the referring level.

Keywords: Norway, Atrial fibrillation, Catheter ablation, Universal health care, Socioeconomic factors, Small-area analysis

Background

Atrial fibrillation (AF) is the most common cardiac arrhythmia, with significant influence on quality of life, morbidity and mortality [1–6]. The prevalence of AF has been increasing over the last decades, and is expected to increase further over the next 30 to 50 years [2, 7–10]. Thus, AF has become an important public health issue and a significant contributor to health care cost in the Western world.

Over the last two decades, catheter ablation has evolved as an important treatment option for many patients with symptomatic AF, with reasonable success rates, low complication rates and acceptable cost-effectiveness [3, 5, 11]. The procedure was primarily indicated for patients without structural heart disease, where rhythm control is the strategy of choice and in whom medical therapy has failed [4]. However, more recently, catheter ablation has

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also increasingly been considered as first-line therapy in selected individuals [3, 6, 12, 13].

In 2010 the Norwegian Ministry of Health and Care Services instructed the regional health authorities (RHA) to increase the capacity for catheter ablation of AF, as there was an increasing discrepancy between demand and capacity for catheter ablation in Norway. This led to a substantial increase in the number of radiofrequency ablation procedures performed within the national health care system. By 2013, Norway was near the top in Europe in number of AF ablations performed per million inhabitants [14].

In Norway, only five hospitals are performing AF ablations, one in each of the four RHAs. In addition, one private hospital in the South-East RHA is performing the procedure as a subcontractor for the regional health authority.

Norway has a universal health care system and in-hospital treatment is free of charge. It is a fundamental principle in this system that equal needs should be met by equal services regardless of e.g., socioeconomic status (SES) or place of residence. However, an increasing number of studies indicate that this principle is not adequately met, in Norway as in other Western countries [15–19]. Several studies report socioeconomic differences in utilisation of health care, e.g. relatively wealthy and/or highly educated people visit more specialists and have more access to sophisticated therapies [16–19]. Furthermore, several decades ago Wennberg reported on small area variations in health care delivery, which could not be explained by corresponding variations in need [20]. Geographic variation in access to health care in Norway has been documented in a broad spectrum of services [15, 21, 22], especially by the Norwegian health care Atlases [23].

According to the equity aims of the Norwegian health care system, treatment with catheter ablation of AF should be distributed according to disease prevalence regardless of socioeconomic class and place of residence. The aim of the present study was to analyse whether there are patient related or geographic differences in the use of this procedure among patients diagnosed with AF.

Methods

Study design and data sources

The study population was the complete cohort of all Norwegians, aged 25 to 75, diagnosed with atrial fibrillation by Norwegian hospitals/specialist health care providers, in Norway in the period 1 January 2008 to 31 December 2017. Data from the Norwegian Patient Register (NPR) and Statistics Norway (SSB) were linked by an encrypted serial number derived from the unique 11-digit personal identifier held by all persons living in Norway. The data from NPR included patient demographics (residential information, year of birth and gender), start and end date for the contact, hospital, type of contact, diagnoses and clinical procedures. In Norway, all hospitals submit data to NPR for registration and reimbursement purposes. The data from SSB included income and level of education each year, gender, year of birth, date of death, date of emigration and residential municipality.

Definitions

The data were analysed by survival analysis and the patient age at the year of the first AF diagnosis was used as entry age. Patients' attained age at the year of ablation, death, emigration or end of study period was used as exit age. As the exact date of birth was not available for this study, age at the first AF diagnosis was calculated as the difference between the year of the first AF diagnosis and the year of birth. Attained age was calculated as the difference between the year of exit and the year of birth. Only patients aged 25 to 75 at the year of the first AF diagnosis were included in the study. In addition, 80 years was set as an upper age limit for attained age, with patients older than 80 being censored at the year they became 80.

The AF diagnoses were identified from the International Statistical Classification of Diseases and Related Health Problems (ICD-10) diagnosis code: I48 (primary or secondary diagnosis). The code I48 also includes atrial flutter, as it was not possible to distinguish between atrial fibrillation and flutter by diagnosis code before 2013. However, atrial fibrillation is a much more common condition than atrial flutter. The AF ablation procedures were identified from the Nomesco Classification of Surgical Procedures (NCSP) code: (FPB32, FPB22, FPB35, FPB25, FPO25A, FPO10A, FPB13). Patients without an AF diagnosis prior to or at the same date as the AF ablation procedure were excluded.

Educational level was coded applying the international standard classification of education (ISCED) [24]. Larger numbers represented higher educational levels; 0 represented less than primary education, and 8 indicated a doctorate or equivalent while 9 was not classified and regarded as missing. Educational level was recoded into three categories; low (0-2), medium (3-5), and high (6-8), where 3-5 is high school level.

After-tax income was calculated as total income minus assessed tax and negative transfers, with total income representing the sum of income as employee, income from self-employment, property income, capital income, and transfers received. The after-tax income was index-adjusted, to 2015 by the consumer price index (CPI), to account for inflation. From after-tax income a categorical income variable was defined with three categories; low (less than NOK 240 000), medium (NOK 240 000 - 400 000), and high (more than NOK 400 000).

The patients' hospital referral area was defined by place of residence and the corresponding geographic catchments areas served by the 21 Norwegian hospital trusts (HT). The patients' regional referral area was defined by the catchment areas for the four regional health authorities (RHA) (North, Central, West and South-East) in Norway. The catchments areas are given by the health authority as administrative borders.

Follow-up time was defined as the number of years from the first AF diagnosis to ablation or censoring. Age, place of residence, income, and educational level were defined according to the date of the first AF diagnosis. Patients with date of censoring equal to date of diagnosis were excluded.

Statistical analyses

Data were analysed using SAS 9.4 (SAS Institute, Cary NC).

Survival analysis was carried out, separately for females and males, by Cox regression with attained age as time scale. Two models were analysed. In model 1, place of residence was classified by the 21 hospital referral areas (HT). In model 2, place of residence was classified by the four regional referral areas (RHA). Apart from this the two models were identical. Age at the first AF diagnosis was treated as entry age to the study, regarded as left truncation time. AF ablation was considered as the relevant event, with educational level, income level, place of residence (hospital (HT) or regional referral area (RHA)) and follow-up time since the first AF diagnosis as covariates. Follow-up time was time-dependent, while the other covariates were defined by the year of the first AF diagnosis. The categories representing low levels of education and income, Vestre Viken (HT) hospital referral area, South-East (RHA) regional referral area, and follow-up time within the first year were set as reference categories. Vestre Viken HT and South-East RHA have the largest number of AF patients in hospital (HT) and regional referral areas (RHA), respectively. The Efron method was applied for handling ties.

In the initial analysis, travel time to hospital was included as a covariate. Two different measures of travel time were applied, travel time to nearest hospital and travel time to nearest ablation hospital. Travel time was measured as travel time by road from municipality centre. Including travel time as a covariate did not have any impact on the remaining results, and this variable was therefore not included in the analysis.

The proportional hazard assumption was tested by generating time dependent covariates by including interactions of the predictors (education, income and place of residence) and the log of attained age in the model, as described in Allison [25], where significant interaction terms indicate non-proportional hazards.

Spearman's rank correlation coefficients were computed in order to investigate associations between the variables representing age group, education and income, separately by gender.

In addition, separate analyses for three different time periods were conducted, for the period before the presumed capacity increase (2008-2010), for the period after the instructed capacity increase (2011-2017), and the period 2013-2017. From 2013, it was possible to distinguish between atrial fibrillation and atrial flutter by ICD-10 codes. Only atrial fibrillation patients with diagnosis codes I48.0, I48.1, and I48.2 were included in the analysis for the period 2013-2017.

Results

Patient selection and characteristics

During 2008-2017, a total of 88 534 patients aged 25–75 years were diagnosed with AF, 29 233 women (mean age at diagnosis 64.6 years) and 59 301 men (mean age at diagnosis 63.0 years) (Table 1). A total of 10 725 patients were treated with ablation in the period, 2 759 women (mean age at ablation 61.1 years) and 7 966 men (mean age at ablation 59.5 years). While 67.0 % of the AF patients were males, 74.3 % of the ablation patients were males. More than half of the AF patients (51.1%) were in the age group 70-75, compared to only 17.6% of the ablation patients in the age group 70-75. Among the AF patients, 27.1% were in the high educational level group, compared to 37.3% among the ablation patients. Of the AF patients, 22.7% belonged to the high income group, compared to 38.8% of the ablation patients. Figure 1 and Table 1 shows the proportion of AF patients treated with ablation in the hospital referral areas. AF patients in Finnmark HT hospital referral area had the lowest proportion (7.1%) treated with ablation, while AF patients in St. Olavs HT hospital referral area had the highest proportion (20.1%).

Results from statistical analysis

Figure 2 shows that a higher proportion of male AF patients were treated with ablation compared to female AF patients, and this was consistent in all age groups and follow-up years. However, the gender differences decreased with increasing age, and in the age groups 60-69 and 70-75 the differences were small.

The rate of ablation, in both female and male AF patients, increased with increasing levels of education. The effect of education was stronger in males than females. Patients with high level of education had around 60% (males) and 35% (females) higher rate of ablation, compared to patients with low education (Table 2).

The rate of ablation in AF patients also increased with increasing levels of income. Similarly, as for education, the effect of income was stronger in males than females, with around 80% (males) and 40% (females) higher rate

Table 1 Characteristics of AF patients and ablation patients. Norway, 2008-2017

	Atrial fibrillation			Ablation (% proportion with ablation)		
	Female	**Male**	**Total**	**Female**	**Male**	**Total**
Number of patients	29 233	59 301	88 534	2 759 (9.4%)	7 966 (13.4%)	10 725 (12.1%)
Age at diagnosis, mean [SD]	64.6 [9.9]	63.0 [9.8]	63.6 [9.8]	59.1 [10.6]	57.7 [10.0]	58.0 [10.2]
Age at exit†, mean [SD]	68.1 [10.4]	66.7 [10.3]	67.1 [10.4]	61.1 [11.1]	59.5 [10.2]	59.9 [10.5]
Years to exit†, mean [SD]	3.5 [2.7]	3.6 [2.8]	3.6 [2.8]	1.9 [2.1]	1.9 [2.1]	1.9 [2.1]
Age group‡						
25-49	2 041	4 458	6 499	430 (21.1%)	1 283 (28.8%)	1 713 (26.4%)
50-59	2 879	7 867	10 746	550 (19.1%)	2 204 (28.0%)	2 754 (25.6%)
60-69	7 651	18 359	26 010	1 143 (14.9%)	3 224 (17.6%)	4 367 (16.8%)
70-75	16 662	28 617	45 279	636 (3.8%)	1 255 (4.4%)	1 891 (4.2%)
Education‡						
Low	8 580	13 232	21 812	563 (6.6%)	1 142 (8.6%)	1 705 (7.8%)
Medium	13 643	29 122	42 765	1 313 (9.6%)	3 705 (12.7%)	5 018 (11.7%)
High	7 010	16 947	23 957	883 (12.6%)	3 119 (18.4%)	4 002 (16.7%)
Income‡						
Low	14 315	10 861	25 176	1 004 (7.0%)	745 (6.9%)	1 749 (6.9%)
Medium	12 156	31 108	43 264	1 339 (11.0%)	3 506 (11.3%)	4 845 (11.2%)
High	2 762	17 332	20 094	416 (15.1%)	3 715 (21.4%)	4 131 (20.6%)
Hospital referral area (HT)‡ ∗						
Finnmark (N)	326	847	1 173	15 (4.6%)	68 (8.0%)	83 (7.1%)
UNN (N)±	977	2 183	3 160	55 (5.6%)	239 (10.9%)	294 (9.3%)
Nordland (N)	765	1 714	2 479	36 (4.7%)	178 (10.4%)	214 (8.6%)
Helgeland (N)	528	1 086	1 614	45 (8.5%)	112 (10.3%)	157 (9.7%)
Nord-Trøndelag (C)	732	1 555	2 287	66 (9.0%)	214 (13.8%)	280 (12.2%)
St. Olavs (C)±	1 390	3 188	4 578	211 (15.2%)	707 (22.2%)	918 (20.1%)
Møre-Romsdal (C)	1 254	2 809	4 063	158 (12.6%)	425 (15.1%)	583 (14.3%)
Førde (W)	590	1 350	1 940	48 (8.1%)	140 (10.4%)	188 (9.7%)
Bergen (W)±	1 959	4 472	6 431	223 (11.4%)	744 (16.6%)	967 (15.0%)
Fonna (W)	924	2 098	3 022	115 (12.4%)	335 (16.0%)	450 (14.9%)
Stavanger (W)	3 326	5 180	8 506	198 (6.0%)	526 (10.2%)	724 (8.5%)
Østfold (SE)	1 689	3 391	5 080	144 (8.5%)	417 (12.3%)	561 (11.0%)
Akershus (SE)∓	2 808	5 253	8 061	257 (9.2%)	673 (12.8%)	930 (11.5%)
OUS (SE)±	1 224	2 597	3 821	131 (10.7%)	398 (15.3%)	529 (13.8%)
Lovisenberg (SE)	368	775	1 143	45 (12.2%)	106 (13.7%)	151 (13.2%)
Diakonhjemmet (SE)	613	1 378	1 991	70 (11.4%)	231 (16.8%)	301 (15.1%)
Innlandet (SE)	2 497	4 992	7 489	179 (7.2%)	487 (9.8%)	666 (8.9%)
Vestre Viken (SE)	2 884	5 714	8 598	334 (11.6%)	825 (14.4%)	1 159 (13.5%)
Vestfold (SE)	1 567	2 975	4 542	139 (8.9%)	358 (12.0%)	497 (10.9%)
Telemark (SE)	1 103	2 302	3 405	125 (11.3%)	343 (14.9%)	468 (13.7%)
Sørlandet (SE)	1 709	3 442	5 151	165 (9.7%)	440 (12.8%)	605 (11.7%)

†Exit is ablation, death, emigration or end of study period. For ablation patients the exit is ablation. ‡ At the time of diagnosis. ∗ The four regional health authorities: *N* North, *C* Central, *W* West and *SE* South-East. ± Hospital trust (HT) with ablation centre. ∓ Location of private ablation centre

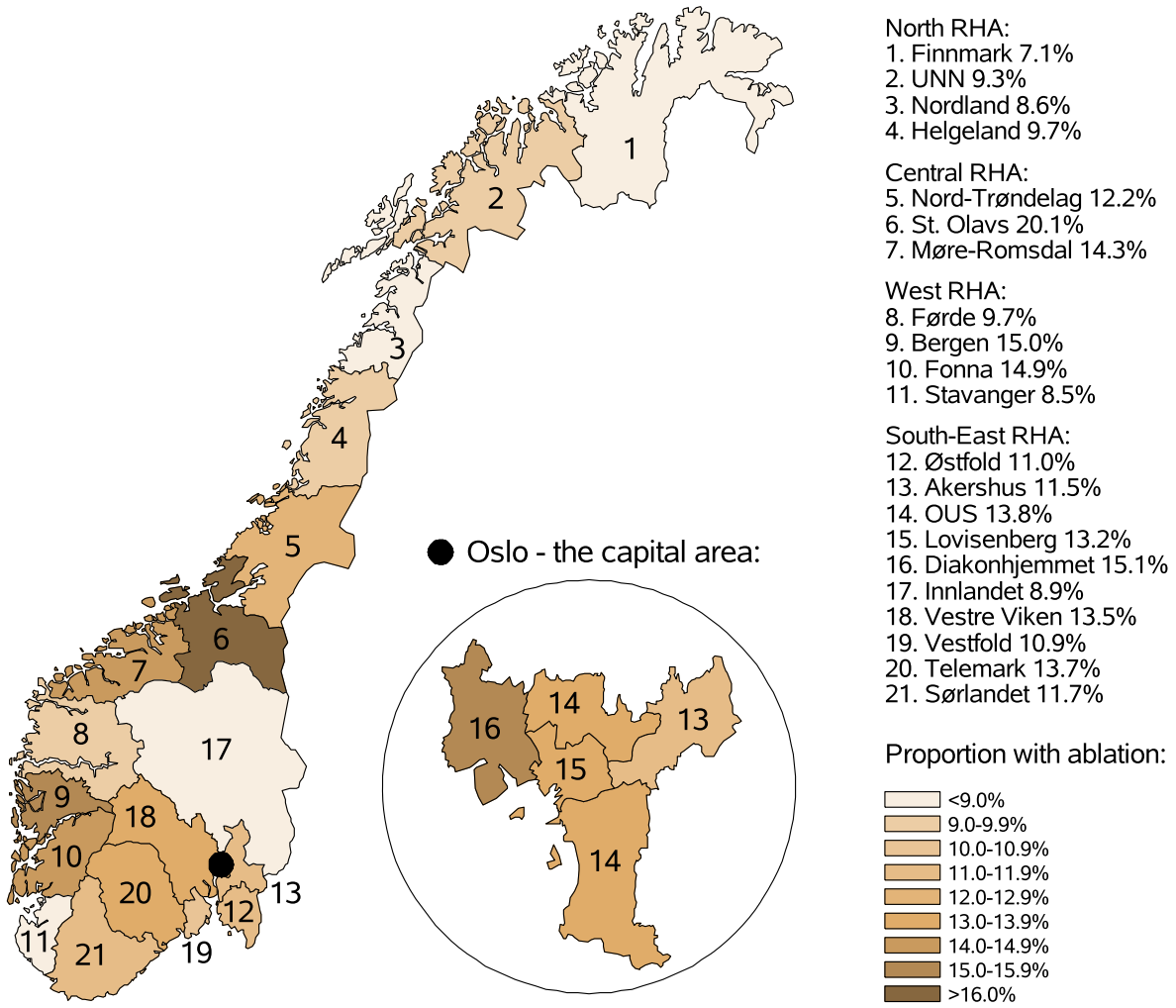

Fig. 1 Proportion of atrial fibrillation patients treated with ablation in the 21 hospital referral areas (HTs) in Norway

of ablation in patients with high income, compared to patients of the same gender with low income.

Compared to patients living in the regional referral area of the South-East RHA, patients living in the regional referral area of the Central RHA had around 50% higher rates of ablation, and patients living in the regional referral area of the North RHA had lower rates of ablation (39% lower for females and 17% lower for males). There was substantial variation within the RHAs. Patients living in the four hospital referral areas in the North RHA all had lower rates of ablation, compared to patients living in the hospital referral area of Vestre Viken HT. Patients living in the hospital referral area of St. Olavs HT, in the Central RHA, had the highest rates of ablation in the country, and around three times as high ablation rates, compared to patients living in the hospital referral area of Finnmark HT (3.9 times higher in females and 2.9 times higher in males).

The rate of ablation decreased with increasing number of years since AF diagnosis in both males and females in both models; however, the decreasing trend was not consistent throughout all the follow-up years.

The tests for proportional hazard showed significant interactions with attained age for education in both females and males and place of residence in females (Table 2). Thus, the effects of education in both genders and the effects of place of residence in females may differ over age groups. This was confirmed by the results from multivariable Cox regressions, separate by both gender and age groups (Tables 3 and 4). In females, the positive effect of education was found in the age groups 50-59, 60-69 and 70-75, and the effect of high educational level

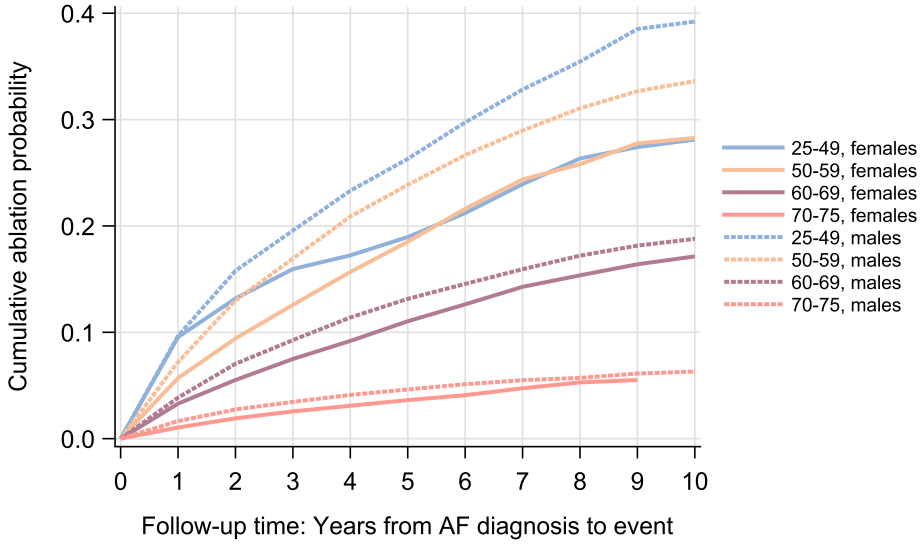

Fig. 2 Cumulative ablation probability by follow-up time, separate by age groups (age at AF diagnosis) and gender. Smooth probability curves

increased with increasing age. In contrast, there was no effect in the age group 25-49. In males, the positive education effect was found in all age groups, and the effect of high educational level increased with increasing age.

The hazard ratios increased with age in patients living in the West (both females and males) and Central (females) RHA, compared to patients living in the South-East RHA (Table 3). This age effect was also present in females living in Bergen and Fonna HT (both in West RHA), compared to patients living in Vestre Viken HT (Table 4).

The correlation coefficients between covariates were relatively low, except for the correlation between education and income (see supplementary Table A1). Cox regression analysis without SES adjustment gave similar results for the HTs and RHAs as in Table 2 (see supplementary, Table A2). The results from the analysis of the three different periods were generally similar to the results in the main analysis (see supplementary).

Discussion

Principal findings

Our data show substantial socioeconomic and geographic differences in frequency of ablation therapy in patients with diagnosed atrial fibrillation in Norway. AF patients living in the regional referral area of the Central RHA had the highest ablation rates, while patients living in the regional referral area of the North RHA were less likely to receive ablation treatment. AF patients with high level of education and high level of income were more frequently treated with ablation.

Age

We found a marked age effect, with younger patients being more likely to receive ablation than older patients. The European guidelines for treatment of atrial fibrillation from 2010 recommend ablation for younger patients with symptomatic paroxysmal or persistent atrial fibrillation in whom antiarrhythmic drug treatment failed [4]. In an update from 2012, these indications were further strengthened [5]. The prevalence of AF increases progressively with age, and age is an independent risk factor for adverse outcomes in AF. AF catheter ablation may be an effective and safe option in selected older individuals with success rates comparable to younger patients [26]. However, age may be a predictor of complications in AF ablation [27] and a longer follow-up study suggests an age-related increase in risk of AF recurrence, major adverse cardiac events, and death after ablation [28].

Gender

Our data showed that females are treated with ablation for atrial fibrillation to a lesser extent than males. This is in line with other studies [29–31]. Females are referred for AF catheter ablation later than males, possibly reflecting AF occurrence later in life among females [32]. Female atrial fibrillation patients more commonly present comorbidities and are referred to hospital care later and with longer disease history [29]. This might affect the clinicians' decisions concerning therapeutic strategy [29]. A review recommends a gendered management strategy in treating AF, as the gender differences in AF are substantial, and antiarrhythmic drugs and ablation can have more complications in females than in males [30]. However, both the 2020 ESC Guidelines and a recent review recommend that females and males are offered diagnostic assessment and therapies equally [6, 33]. It is difficult to conclude on gender differences in risk and benefit of different treatment strategies in AF patients, as females

Table 2 Multivariable Cox regression, separate by gender. Hazard ratios (95% confidence interval), adjusted for follow-up time

	Model 1 (HT)			**Model 2 (RHA)**	
	Female	**Male**		**Female**	**Male**
Education			**Education**		
Low	1.0 (ref)	1.0 (ref)	Low	1.0 (ref)	1.0 (ref)
Medium	1.31 (1.19 - 1.45)	1.28 (1.20 - 1.37)	Medium	1.32 (1.19 - 1.45)	1.29 (1.21 - 1.38)
High	1.34 (1.19 - 1.51)	1.62 (1.51 - 1.74)	High	1.36 (1.21 - 1.53)	1.67 (1.55 - 1.79)
Income			**Income**		
Low	1.0 (ref)	1.0 (ref)	Low	1.0 (ref)	1.0 (ref)
Medium	1.20 (1.10 - 1.31)	1.54 (1.42 - 1.67)	Medium	1.20 (1.10 - 1.31)	1.54 (1.42 - 1.67)
High	1.40 (1.23 - 1.59)	1.84 (1.69 - 2.00)	High	1.37 (1.21 - 1.56)	1.82 (1.68 - 1.97)
Follow-up time (years)			**Follow-up time (years)**		
1	1.0 (ref)	1.0 (ref)	1	1.0 (ref)	1.0 (ref)
2	0.68 (0.61 - 0.76)	0.86 (0.81 - 0.91)	2	0.68 (0.61 - 0.75)	0.85 (0.80 - 0.91)
3	0.63 (0.56 - 0.71)	0.64 (0.60 - 0.69)	3	0.63 (0.56 - 0.71)	0.64 (0.59 - 0.69)
4	0.58 (0.51 - 0.67)	0.70 (0.65 - 0.75)	4	0.58 (0.50 - 0.66)	0.70 (0.64 - 0.75)
5	0.68 (0.59 - 0.79)	0.62 (0.56 - 0.68)	5	0.68 (0.58 - 0.79)	0.62 (0.56 - 0.67)
6	0.73 (0.61 - 0.86)	0.63 (0.57 - 0.70)	6	0.73 (0.61 - 0.87)	0.63 (0.57 - 0.70)
7	0.85 (0.71 - 1.03)	0.63 (0.56 - 0.71)	7	0.86 (0.71 - 1.03)	0.63 (0.56 - 0.71)
8	0.63 (0.49 - 0.82)	0.62 (0.53 - 0.71)	8	0.64 (0.49 - 0.82)	0.62 (0.53 - 0.72)
9	0.62 (0.45 - 0.86)	0.59 (0.49 - 0.71)	9	0.63 (0.45 - 0.86)	0.59 (0.49 - 0.71)
10 or more	0.37 (0.21 - 0.66)	0.33 (0.24 - 0.46)	10 or more	0.37 (0.21 - 0.66)	0.33 (0.24 - 0.46)
Hospital referral area (HT)			**Regional referral area (RHA)**		
Finnmark (N)	0.39 (0.23 - 0.66)	0.62 (0.48 - 0.80)	North	0.61 (0.52 - 0.72)	0.83 (0.76 - 0.90)
UNN (N)	0.52 (0.39 - 0.69)	0.81 (0.70 - 0.94)	Central	1.43 (1.29 - 1.59)	1.52 (1.43 - 1.62)
Nordland (N)	0.45 (0.32 - 0.63)	0.82 (0.70 - 0.97)	West	0.79 (0.72 - 0.87)	1.01 (0.95 - 1.07)
Helgeland (N)	0.73 (0.53 - 1.00)	0.80 (0.66 - 0.97)	South-East	1.0 (ref)	1.0 (ref)
Nord-Trøndelag (C)	0.86 (0.66 - 1.12)	1.14 (0.98 - 1.32)			
St. Olavs (C)	1.50 (1.26 - 1.78)	1.78 (1.61 - 1.97)			
Møre-Romsdal (C)	1.19 (0.99 - 1.44)	1.24 (1.10 - 1.39)			
Førde (W)	0.81 (0.60 - 1.10)	0.83 (0.70 - 1.00)			
Bergen (W)	1.09 (0.92 - 1.29)	1.27 (1.15 - 1.40)			
Fonna (W)	1.18 (0.96 - 1.47)	1.29 (1.13 - 1.46)			
Stavanger (W)	0.38 (0.32 - 0.46)	0.65 (0.58 - 0.72)			
Østfold (SE)	0.84 (0.69 - 1.02)	0.95 (0.85 - 1.07)			
Akershus (SE)	0.81 (0.69 - 0.96)	0.94 (0.85 - 1.04)			
OUS (SE)	0.90 (0.73 - 1.10)	1.00 (0.89 - 1.13)			
Lovisenberg (SE)	0.97 (0.71 - 1.32)	0.90 (0.73 - 1.10)			
Diakonhjemmet (SE)	0.91 (0.70 - 1.17)	1.02 (0.88 - 1.18)			
Innlandet (SE)	0.67 (0.56 - 0.81)	0.80 (0.71 - 0.89)			
Vestre Viken (SE)	1.0 (ref)	1.0 (ref)			
Vestfold (SE)	0.78 (0.64 - 0.95)	0.87 (0.77 - 0.99)			
Telemark (SE)	1.05 (0.86 - 1.29)	1.13 (1.00 - 1.28)			
Sørlandet (SE)	0.90 (0.74 - 1.08)	0.98 (0.87 - 1.10)			
Interactions with attained age (p-values)			**Interactions with attained age (p-values)**		
Education	<0.001	<0.001	Education	<0.001	0.001
Income	0.53	0.17	Income	0.85	0.06
Area (HT)	<0.001	0.50	Area (RHA)	<0.001	0.25

Table 3 Multivariable Cox regression, Model 2 (RHA), adjusted for follow-up time. Separate by gender and age groups (age at AF diagnosis). Hazard ratios (95% confidence interval)

	All	25-49	50-59	60-69	70-75
Female					
Education					
Low	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
Medium	1.32 (1.19 - 1.45)	1.21 (0.94 - 1.57)	1.28 (1.04 - 1.57)	1.28 (1.11 - 1.49)	1.54 (1.19 - 1.98)
High	1.36 (1.21 - 1.53)	1.01 (0.77 - 1.33)	1.28 (1.02 - 1.61)	1.54 (1.29 - 1.84)	1.63 (1.17 - 2.27)
Income					
Low	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
Medium	1.20 (1.10 - 1.31)	1.14 (0.90 - 1.44)	1.31 (1.09 - 1.58)	1.13 (0.99 - 1.28)	1.23 (0.98 - 1.55)
High	1.37 (1.21 - 1.56)	1.45 (1.09 - 1.93)	1.35 (1.05 - 1.73)	1.33 (1.09 - 1.62)	1.60 (1.01 - 2.55)
Regional referral area (RHA)					
North	0.61 (0.52 - 0.72)	0.51 (0.34 - 0.77)	0.60 (0.43 - 0.84)	0.65 (0.51 - 0.84)	0.69 (0.44 - 1.08)
Central	1.43 (1.29 - 1.59)	1.01 (0.75 - 1.38)	1.15 (0.92 - 1.44)	1.67 (1.44 - 1.95)	1.86 (1.41 - 2.45)
West	0.79 (0.72 - 0.87)	0.33 (0.27 - 0.42)	0.74 (0.61 - 0.90)	1.10 (0.95 - 1.27)	1.35 (1.05 - 1.74)
South-East	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
Male					
Education					
Low	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
Medium	1.29 (1.21 - 1.38)	1.37 (1.18 - 1.60)	1.25 (1.12 - 1.41)	1.32 (1.18 - 1.47)	1.23 (0.99 - 1.52)
High	1.67 (1.55 - 1.79)	1.45 (1.23 - 1.70)	1.52 (1.34 - 1.72)	1.82 (1.62 - 2.05)	2.17 (1.72 - 2.73)
Income					
Low	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
Medium	1.54 (1.42 - 1.67)	1.55 (1.28 - 1.88)	1.72 (1.48 - 2.01)	1.39 (1.23 - 1.56)	1.50 (1.20 - 1.88)
High	1.82 (1.68 - 1.97)	1.64 (1.34 - 1.99)	2.05 (1.76 - 2.39)	1.68 (1.49 - 1.91)	1.92 (1.47 - 2.50)
Regional referral area (RHA)					
North	0.83 (0.76 - 0.90)	0.87 (0.72 - 1.06)	0.83 (0.72 - 0.96)	0.80 (0.69 - 0.92)	0.79 (0.58 - 1.07)
Central	1.52 (1.43 - 1.62)	1.50 (1.30 - 1.73)	1.47 (1.31 - 1.64)	1.52 (1.38 - 1.67)	1.78 (1.47 - 2.17)
West	1.01 (0.95 - 1.07)	0.81 (0.71 - 0.92)	0.87 (0.78 - 0.96)	1.20 (1.10 - 1.31)	1.29 (1.07 - 1.55)
South-East	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)

are significantly underrepresented in studies on AF [30]. However, in Norway, the gender differences seem to diminish with age, as the ablation probabilities are almost equal for the older AF patients.

Income and education

Both patients with high level of education and patients with high income were more likely to receive ablation than patients with low level of education and low income. These inequalities increased with increasing age. However, no effect of education was found in the youngest females.

Socioeconomic differences in use of health care services have been discussed extensively, also in countries as Norway with universal health care systems where there is no co-payment from the patients for in-hospital treatment. Our finding, that patients with higher education and higher income are over-represented among those who undergo ablation therapy, is in accordance with several other reports of such gradients in the use of specialised health care, both international and from Norway [16, 17, 34]. For coronary heart disease, socioeconomic differences in revascularisation procedures have been reported in several European countries [35–38]. In a study from Denmark, socioeconomic differences were documented in outcomes after hospital admission for atrial fibrillation or flutter, both in mortality and treatment with ablation [39]. A Norwegian study indicated that low SES was related to higher mortality in AF patients [40].

One of the mechanisms underlying SES differences in health care use may be found in the concept of health literacy [41]. Health literacy is the degree to which individuals have the ability to find, understand, and use information and services to inform health-related decisions and

Table 4 Multivariable Cox regression, Model 1 (HT), adjusted for follow-up time. Separate by gender and age groups (age at AF diagnosis). Hazard ratios (95% confidence interval)

	All	25-49	50-59	60-69	70-75
Female					
Education					
Low	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
Medium	1.31 (1.19 - 1.45)	1.23 (0.95 - 1.60)	1.27 (1.03 - 1.56)	1.28 (1.10 - 1.48)	1.51 (1.17 - 1.94)
High	1.34 (1.19 - 1.51)	1.01 (0.77 - 1.33)	1.26 (1.00 - 1.59)	1.53 (1.28 - 1.83)	1.56 (1.12 - 2.18)
Income					
Low	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
Medium	1.20 (1.10 - 1.31)	1.15 (0.91 - 1.46)	1.33 (1.11 - 1.60)	1.13 (0.99 - 1.29)	1.20 (0.95 - 1.51)
High	1.40 (1.23 - 1.59)	1.52 (1.14 - 2.03)	1.42 (1.10 - 1.82)	1.34 (1.10 - 1.64)	1.54 (0.96 - 2.46)
Hospital referral area (HT)					
Finnmark (N)	0.39 (0.23 - 0.66)	0.44 (0.14 - 1.40)	0.54 (0.22 - 1.32)	0.29 (0.12 - 0.71)	0.43 (0.10 - 1.80)
UNN (N)	0.52 (0.39 - 0.69)	0.72 (0.39 - 1.34)	0.62 (0.35 - 1.10)	0.42 (0.27 - 0.66)	0.52 (0.23 - 1.16)
Nordland (N)	0.45 (0.32 - 0.63)	0.33 (0.10 - 1.05)	0.52 (0.26 - 1.04)	0.44 (0.27 - 0.72)	0.53 (0.23 - 1.25)
Helgeland (N)	0.73 (0.53 - 1.00)	0.29 (0.13 - 0.67)	0.68 (0.34 - 1.35)	1.08 (0.70 - 1.66)	0.90 (0.38 - 2.12)
Nord-Trøndelag (C)	0.86 (0.66 - 1.12)	0.67 (0.32 - 1.40)	0.99 (0.58 - 1.70)	0.90 (0.62 - 1.29)	0.65 (0.28 - 1.54)
St. Olavs (C)	1.50 (1.26 - 1.78)	0.92 (0.56 - 1.51)	1.32 (0.91 - 1.91)	1.61 (1.25 - 2.06)	2.23 (1.45 - 3.43)
Møre-Romsdal (C)	1.19 (0.99 - 1.44)	1.06 (0.63 - 1.77)	1.02 (0.69 - 1.52)	1.32 (1.01 - 1.73)	1.34 (0.79 - 2.26)
Førde (W)	0.81 (0.60 - 1.10)	0.41 (0.15 - 1.12)	0.82 (0.43 - 1.54)	0.94 (0.62 - 1.43)	0.84 (0.38 - 1.87)
Bergen (W)	1.09 (0.92 - 1.29)	0.82 (0.52 - 1.27)	1.18 (0.83 - 1.67)	1.00 (0.78 - 1.29)	1.57 (1.02 - 2.41)
Fonna (W)	1.18 (0.96 - 1.47)	0.78 (0.44 - 1.36)	1.18 (0.74 - 1.88)	1.30 (0.96 - 1.76)	1.38 (0.79 - 2.44)
Stavanger (W)	0.38 (0.32 - 0.46)	0.20 (0.14 - 0.29)	0.43 (0.30 - 0.63)	0.59 (0.44 - 0.78)	0.71 (0.41 - 1.22)
Østfold (SE)	0.84 (0.69 - 1.02)	0.71 (0.43 - 1.17)	0.92 (0.62 - 1.38)	0.90 (0.68 - 1.19)	0.65 (0.36 - 1.18)
Akershus (SE)	0.81 (0.69 - 0.96)	0.91 (0.62 - 1.33)	0.85 (0.61 - 1.19)	0.76 (0.60 - 0.97)	0.80 (0.50 - 1.27)
OUS (SE)	0.90 (0.73 - 1.10)	0.82 (0.52 - 1.31)	1.21 (0.82 - 1.79)	0.77 (0.56 - 1.06)	0.89 (0.50 - 1.59)
Lovisenberg (SE)	0.97 (0.71 - 1.32)	1.16 (0.65 - 2.08)	0.54 (0.23 - 1.23)	1.09 (0.70 - 1.69)	0.56 (0.13 - 2.30)
Diakonhjemmet (SE)	0.91 (0.70 - 1.17)	1.09 (0.60 - 1.99)	0.82 (0.46 - 1.45)	0.70 (0.46 - 1.06)	1.58 (0.88 - 2.82)
Innlandet (SE)	0.67 (0.56 - 0.81)	0.79 (0.52 - 1.21)	0.98 (0.69 - 1.37)	0.48 (0.36 - 0.65)	0.74 (0.44 - 1.22)
Vestre Viken (SE)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
Vestfold (SE)	0.78 (0.64 - 0.95)	0.55 (0.33 - 0.93)	0.96 (0.66 - 1.40)	0.76 (0.56 - 1.02)	0.88 (0.51 - 1.52)
Telemark (SE)	1.05 (0.86 - 1.29)	1.23 (0.78 - 1.93)	1.12 (0.74 - 1.69)	0.99 (0.73 - 1.36)	0.81 (0.44 - 1.52)
Sørlandet (SE)	0.90 (0.74 - 1.08)	0.92 (0.61 - 1.41)	1.23 (0.86 - 1.77)	0.78 (0.58 - 1.04)	0.74 (0.43 - 1.29)
Male					
Education					
Low	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
Medium	1.28 (1.20 - 1.37)	1.34 (1.15 - 1.56)	1.25 (1.11 - 1.40)	1.30 (1.17 - 1.45)	1.22 (0.99 - 1.52)
High	1.62 (1.51 - 1.74)	1.40 (1.19 - 1.65)	1.48 (1.30 - 1.68)	1.78 (1.58 - 2.00)	2.12 (1.68 - 2.68)
Income					
Low	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
Medium	1.54 (1.42 - 1.67)	1.58 (1.30 - 1.92)	1.72 (1.48 - 2.01)	1.38 (1.23 - 1.56)	1.48 (1.18 - 1.85)
High	1.84 (1.69 - 2.00)	1.69 (1.39 - 2.06)	2.07 (1.77 - 2.41)	1.69 (1.49 - 1.91)	1.86 (1.42 - 2.43)
Hospital referral area (HT)					
Finnmark (N)	0.62 (0.48 - 0.80)	0.86 (0.49 - 1.52)	0.49 (0.31 - 0.78)	0.60 (0.41 - 0.88)	0.88 (0.42 - 1.81)
UNN (N)	0.81 (0.70 - 0.94)	1.12 (0.81 - 1.53)	0.92 (0.73 - 1.17)	0.66 (0.51 - 0.84)	0.55 (0.32 - 0.94)
Nordland (N)	0.82 (0.70 - 0.97)	1.01 (0.69 - 1.47)	0.89 (0.68 - 1.18)	0.73 (0.57 - 0.95)	0.62 (0.34 - 1.11)
Helgeland (N)	0.80 (0.66 - 0.97)	0.61 (0.36 - 1.04)	0.88 (0.63 - 1.22)	0.81 (0.59 - 1.10)	0.80 (0.41 - 1.54)
Nord-Trøndelag (C)	1.14 (0.98 - 1.32)	1.45 (1.04 - 2.01)	1.23 (0.94 - 1.62)	0.94 (0.74 - 1.20)	1.09 (0.67 - 1.79)
St. Olavs (C)	1.78 (1.61 - 1.97)	1.87 (1.47 - 2.39)	1.75 (1.46 - 2.09)	1.70 (1.45 - 1.99)	1.99 (1.46 - 2.70)
Møre-Romsdal (C)	1.24 (1.10 - 1.39)	1.46 (1.10 - 1.93)	1.30 (1.06 - 1.60)	1.13 (0.94 - 1.35)	1.10 (0.75 - 1.62)
Førde (W)	0.83 (0.70 - 1.00)	1.16 (0.77 - 1.74)	0.72 (0.52 - 1.01)	0.81 (0.61 - 1.07)	0.80 (0.46 - 1.38)
Bergen (W)	1.27 (1.15 - 1.40)	1.25 (0.98 - 1.59)	1.21 (1.01 - 1.44)	1.30 (1.12 - 1.52)	1.32 (0.97 - 1.80)
Fonna (W)	1.29 (1.13 - 1.46)	1.38 (1.01 - 1.89)	1.15 (0.91 - 1.46)	1.31 (1.08 - 1.59)	1.39 (0.93 - 2.07)

Table 4 Multivariable Cox regression, Model 1 (HT), adjusted for follow-up time. Separate by gender and age groups (age at AF diagnosis). Hazard ratios (95% confidence interval) *(Continued)*

	All	25-49	50-59	60-69	70-75
Stavanger (W)	0.65 (0.58 - 0.72)	0.61 (0.48 - 0.77)	0.60 (0.49 - 0.73)	0.75 (0.63 - 0.90)	0.74 (0.50 - 1.09)
Østfold (SE)	0.95 (0.85 - 1.07)	1.09 (0.83 - 1.44)	0.98 (0.80 - 1.21)	0.83 (0.69 - 1.01)	1.07 (0.74 - 1.54)
Akershus (SE)	0.94 (0.85 - 1.04)	1.13 (0.90 - 1.44)	1.00 (0.84 - 1.20)	0.82 (0.69 - 0.97)	0.87 (0.63 - 1.21)
OUS (SE)	1.00 (0.89 - 1.13)	1.39 (1.08 - 1.80)	1.03 (0.83 - 1.27)	0.86 (0.71 - 1.05)	0.87 (0.58 - 1.31)
Lovisenberg (SE)	0.90 (0.73 - 1.10)	0.83 (0.55 - 1.24)	1.00 (0.70 - 1.44)	1.05 (0.76 - 1.46)	0.49 (0.18 - 1.33)
Diakonhjemmet (SE)	1.02 (0.88 - 1.18)	1.08 (0.76 - 1.53)	1.07 (0.80 - 1.42)	0.95 (0.76 - 1.18)	1.05 (0.68 - 1.62)
Innlandet (SE)	0.80 (0.71 - 0.89)	0.94 (0.72 - 1.23)	0.85 (0.70 - 1.04)	0.74 (0.62 - 0.88)	0.62 (0.42 - 0.90)
Vestre Viken (SE)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
Vestfold (SE)	0.87 (0.77 - 0.99)	0.96 (0.71 - 1.30)	1.05 (0.86 - 1.29)	0.75 (0.62 - 0.92)	0.61 (0.39 - 0.94)
Telemark (SE)	1.13 (1.00 - 1.28)	1.27 (0.95 - 1.69)	1.21 (0.97 - 1.51)	1.11 (0.91 - 1.35)	0.73 (0.45 - 1.16)
Sørlandet (SE)	0.98 (0.87 - 1.10)	1.22 (0.93 - 1.59)	1.08 (0.88 - 1.32)	0.85 (0.70 - 1.02)	0.80 (0.54 - 1.18)

actions for themselves and others [42]. Health literate patients may be more capable of understanding, questioning and discussing treatment options with their physician. It has been demonstrated that low functional health literacy is associated with sub-optimal use of health care services [43], and the association between educational level and health literacy is well documented [44]. A systematic review of associations between socioeconomic status, atrial fibrillation, and outcomes found no consistent social gradient in the risk of AF [45]. However, when AF was present there was a social gradient in the risk of poorer outcome. Low SES was associated with outcomes such as poorer treatment, less knowledge, poorer psychological health and higher mortality.

Demand for a specific treatment depends on the preferences, perceptions and prejudices of both patient and health care provider [46]. Two equally healthy individuals may assess their health differently because their conceptions of good health and their health expectations are contingent on their knowledge of disease and available treatments. More highly educated people are reported to assess their health more negatively, and superior information acquisition skills increase the likelihood that they will recognise and report symptoms of disease earlier [19]. The socioeconomic gradient in physical activity is well known, and individuals in higher SES classes are more likely to be physically active compared to individuals in lower SES classes [47, 48]. Even though physical activity improves the health of AF patients, it is also reported that exercise can trigger AF episodes in paroxysmal AF patients [49]. Thus, AF patients in higher SES classes might be more affected by AF, and may therefore both prefer and demand ablation treatment to a greater extent than AF patients in lower SES classes. However, several studies have shown that exercise can reduce the burden of AF [50–52].

Follow-up time

The rate of ablation decreased with time since the AF diagnosis. This is as expected, as the natural history of AF is characterised by progressive atrial remodelling. Shorter duration between the time of first AF diagnosis and AF ablation is associated with an increased likelihood of ablation procedural success [53]. The atrial substrate and remodelling increase with the duration of ongoing AF and lead to greater resistance to successful AF ablation, and higher AF recurrence rates [53].

Geographic variation

Substantial geographic variation was found in the probability of ablation according to the patients' place of residence, both considering hospital referral areas (HT) and regional referral areas (RHA).

Geographic variation in ablation utilisation has been documented in studies from both Europe and the US [54, 55]. Also among Medicare beneficiaries in the US, marked geographic variation in the use of catheter ablation for atrial fibrillation has been found. The variation was not associated with the prevalence of atrial fibrillation, availability of cardiologists or end-of-life resource use [56].

Unwarranted variation in health care is mainly due to services that can be defined as preference-sensitive or supply-sensitive [57]. Preference-sensitive care represents patient preferences, clinical practice, and preferences and beliefs of a single clinician or department rather than a clear evidence-based approach. Supply-sensitive care refers to local capacity of health care resources, such as ablation clinics. The observed geographic variation in this study is probably related to both differences in clinical practice and differences in capacity.

The reasons for the observed variation in the ablation rate are not clear but may reflect provider preferences and uncertainty of safety and/or efficacy of the procedure in a region. Ablation for atrial fibrillation is a procedure that is developing fast. The rapid development in procedural techniques and indications may increase the likelihood that specialists performing the procedure show individual variation in patient selection. Some specialists might pri-

marily select patients without structural heart disease who have highly symptomatic, paroxysmal atrial fibrillation and have failed one or more treatments with antiarrhythmic drugs. Others might have a different threshold and offer ablation as first-line therapy, or to patients with persistent or chronic fibrillation, with or without underlying structural heart disease. Guidelines might be implemented at different time points in the regions, as the shift in ablation probability between age groups in West RHA might be an example of. Furthermore, not all primary care and local hospital physicians, who are responsible for referring the patients to specialists in Norway, may be equally familiar with the potential benefit of the procedure.

Differences in ablation capacity at the five ablation centres can also contribute to the observed geographic variation. The ablation procedure in Norway was first implemented in 2001 in the West RHA, while the North RHA was the last RHA to implement the procedure in 2009. The waiting time for ablation has been more than a year during the study period, despite the fact that all five ablation centres have fully utilised the capacity. However, ablation capacity cannot alone explain the threefold difference in rates of ablation between patients living in the hospital referral areas of Finnmark HT and St. Olavs HT.

Differences in sociodemographic factors between the hospital referral areas might be a source of variation. However, the funding system for public hospitals in Norway is based on a model that accounts for regional differences in sociodemographic factors and differences in the cost of providing specialist health care services. The aim of the model is to ensure equitable health care services across the regions.

Strengths and limitations

The major strength of this study is that it covers, for all practical purposes, all patients who have been diagnosed with atrial fibrillation within the specialised health care services and all patients who have undergone ablation within the national health care system in Norway during the period 2008-2017. We have information about income and educational level of all patients included in the study. Privately financed ablations are not included, as there are no available data on privately financed procedures in Norway. However, the vast majority of Norwegian health care services are publicly financed, and this is, even more, the case for ablations. Thus, there are no reasons to believe that this limitation is important for the interpretation of our data.

During the study period, the guidelines for treatment of AF patients have evolved, and the results should be interpreted in accordance with the applicable guidelines at any given time. The ICD-10 code I48 for atrial fibrillation was used to identify the patient population in this study. A possible limitation is that this also includes atrial flutter. Until 2013 it was not possible to distinguish between atrial fibrillation and atrial flutter. This means that the actual number of atrial fibrillation patients is somewhat lower than reported. However, the separate analysis for the period 2013-2017, with atrial fibrillation patients only, showed similar associations.

Individuals moving between residential areas within the study period could be a limitation. However, this will probably have a small effect, since the study population is older and less people tend to move compared to younger people.

The test for the proportional hazard assumption and the separate analysis for age groups showed that some of the effects varied over age groups. Interpretation of the results must take this age effect into consideration.

Conclusion

This study demonstrates a significant socioeconomic gradient in the proportion of AF patients treated with ablation in Norway. This gradient is probably related to both differences in health literacy and differences in patient preference and demands between socioeconomic groups. Further research exploring the mechanisms by which SES influences the choice of treatment of AF patients is warranted. A substantial part of the geographic variation is probably related to differences in capacity. However, geographic variation caused by differences in clinical practice and provider preferences implies a need for clearer guidelines, both at specialist level and also at the referring level. The observed gender differences in ablation probabilities, especially in younger AF patients, do not necessarily reflect differences in AF morbidity only but also differences in clinical strategies. More research on gender differences in the effect of treatment strategies is needed.

Abbreviations

AF: Atrial fibrillation; HT: Hospital trust; ICD-10: International Statistical Classification of Diseases and Related Health Problems diagnosis codes; ISCED: International standard classification of education; NCSP: Nomesco Classification of Surgical Procedures codes NPR: Norwegian Patient Registry; RHA: Regional health authority; SES: Socioeconomic status; SSB: Statistics Norway

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12889-022-12628-9.

Additional file 1: Supplementary tables.

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Authors' contributions
F.O., L.B., B.U., P.M.T. and E.B. conceived and designed the study. F.O. facilitated and analysed the data. F.O., B.K.J. and I.H. contributed to the analytical strategy. F.O., L.B., E.B. and B.K.J. drafted the manuscript. All authors participated in the revision of the manuscript. The authors read and approved the final manuscript.

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Availability of data and materials
The data that support the findings of this study are available from the Norwegian Patient Registry (NPR) and the Statistics Norway (SSB), but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of the NPR and the SSB.

Declarations

Ethics approval and consent to participate
The study is based on secondary use of data from clinical and administrative registries. The Regional Committees for Medical and Health Research Ethics of South East region (REC South East A) has given exemption from the duty of confidentiality, and exempted from ethical approval and need of informed consent (ref. 20627/REC South East A). The project has conducted a Data Protection Impact Assessment (DPIA). All methods were performed in accordance with the relevant guidelines and regulations.

Consent for publication
Not required.

Competing interests
None declared.

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Publisher's Note

Supplementary

Table A1: Correlations, Spearman rank correlation.

		Age group	Education	Income
Females	Age group	1	-0.164	-0.265
	Education	-0.164	1	0.430
	Income	-0.265	0.430	1
Males	Age group	1	-0.071	-0.232
	Education	-0.071	1	0.376
	Income	-0.232	0.376	1

Table A2: Multivariable Cox regression without SES, separate by gender. Hazard ratios (95% confidence interval), adjusted for follow-up time.

	Model 1 (HT)			Model 2 (RHA)	
	Female	Male		Female	Male
Follow-up time (years)			**Follow-up time (years)**		
1	1.0 (ref)	1.0 (ref)	1	1.0 (ref)	1.0 (ref)
2	0.68 (0.61 - 0.76)	0.86 (0.81 - 0.91)	2	0.68 (0.61 - 0.76)	0.85 (0.80 - 0.91)
3	0.63 (0.56 - 0.72)	0.64 (0.60 - 0.69)	3	0.63 (0.56 - 0.71)	0.64 (0.59 - 0.69)
4	0.59 (0.51 - 0.67)	0.70 (0.65 - 0.75)	4	0.58 (0.51 - 0.67)	0.70 (0.64 - 0.75)
5	0.68 (0.59 - 0.79)	0.61 (0.56 - 0.67)	5	0.68 (0.59 - 0.79)	0.61 (0.56 - 0.67)
6	0.73 (0.61 - 0.86)	0.63 (0.56 - 0.70)	6	0.73 (0.61 - 0.87)	0.63 (0.56 - 0.70)
7	0.85 (0.71 - 1.03)	0.62 (0.55 - 0.71)	7	0.85 (0.71 - 1.03)	0.63 (0.55 - 0.71)
8	0.63 (0.49 - 0.82)	0.61 (0.53 - 0.71)	8	0.64 (0.49 - 0.82)	0.62 (0.53 - 0.72)
9	0.63 (0.45 - 0.86)	0.59 (0.49 - 0.71)	9	0.63 (0.46 - 0.87)	0.59 (0.49 - 0.71)
10 or more	0.38 (0.21 - 0.67)	0.33 (0.24 - 0.46)	10 or more	0.38 (0.21 - 0.67)	0.34 (0.24 - 0.47)
Hospital referral area (HT)			**Regional referral area (RHA)**		
Finnmark (N)	0.39 (0.23 - 0.66)	0.55 (0.43 - 0.70)	North	0.60 (0.51 - 0.71)	0.76 (0.70 - 0.83)
UNN (N)	0.49 (0.37 - 0.65)	0.73 (0.63 - 0.85)	Central	1.42 (1.27 - 1.58)	1.47 (1.39 - 1.57)
Nordland (N)	0.43 (0.31 - 0.61)	0.72 (0.62 - 0.85)	West	0.80 (0.72 - 0.88)	1.01 (0.95 - 1.07)
Helgeland (N)	0.70 (0.51 - 0.96)	0.68 (0.56 - 0.82)	South-East	1.0 (ref)	1.0 (ref)
Nord-Trøndelag (C)	0.82 (0.63 - 1.06)	1.02 (0.87 - 1.18)			
St. Olavs (C)	1.47 (1.24 - 1.75)	1.69 (1.53 - 1.86)			
Møre-Romsdal (C)	1.15 (0.95 - 1.39)	1.14 (1.02 - 1.28)			
Førde (W)	0.78 (0.58 - 1.06)	0.76 (0.63 - 0.91)			
Bergen (W)	1.06 (0.90 - 1.26)	1.22 (1.11 - 1.35)			
Fonna (W)	1.14 (0.92 - 1.41)	1.20 (1.06 - 1.36)			
Stavanger (W)	0.38 (0.32 - 0.45)	0.64 (0.57 - 0.71)			
Østfold (SE)	0.78 (0.64 - 0.95)	0.86 (0.77 - 0.97)			
Akershus (SE)	0.81 (0.68 - 0.95)	0.90 (0.81 - 1.00)			
OUS (SE)	0.92 (0.75 - 1.13)	1.03 (0.91 - 1.16)			
Lovisenberg (SE)	0.96 (0.71 - 1.32)	0.87 (0.71 - 1.06)			
Diakonhjemmet (SE)	1.01 (0.78 - 1.30)	1.17 (1.01 - 1.35)			
Innlandet (SE)	0.64 (0.53 - 0.77)	0.71 (0.63 - 0.79)			
Vestre Viken (SE)	1.0 (ref)	1.0 (ref)			
Vestfold (SE)	0.75 (0.62 - 0.91)	0.83 (0.73 - 0.94)			
Telemark (SE)	1.00 (0.82 - 1.23)	1.04 (0.92 - 1.18)			
Sørlandet (SE)	0.86 (0.71 - 1.04)	0.92 (0.82 - 1.03)			

B: 2008-2010 - Before capacity increase

Table B1: Characteristics of patients 2008-2010.

	Atrial fibrillation			Ablation (% proportion with ablation)		
	Female	Male	Total	Female	Male	Total
Number of patients	7 844	17 949	25 793	287 (3.7%)	1 139 (6.3%)	1 426 (5.5%)
Age group‡						
Under 50	456	1 538	1 994	49 (10.7%)	230 (15.0%)	279 (14.0%)
50-59	966	3 445	4 411	86 (8.9%)	364 (10.6%)	450 (10.2%)
60-69	3 307	7 873	11 180	123 (3.7%)	441 (5.6%)	564 (5.0%)
70 and older	3 115	5 093	8 208	29 (0.9%)	104 (2.0%)	133 (1.6%)
Education‡						
Low	2 647	4 128	6 775	68 (2.6%)	155 (3.8%)	223 (3.3%)
Medium	3 603	8 736	12 339	123 (3.4%)	537 (6.1%)	660 (5.3%)
High	1 594	5 085	6 679	96 (6.0%)	447 (8.8%)	543 (8.1%)
Income‡						
Low	4 761	4 145	8 906	126 (2.6%)	134 (3.2%)	260 (2.9%)
Medium	2 611	8 842	11 453	131 (5.0%)	508 (5.7%)	639 (5.6%)
High	472	4 962	5 434	30 (6.4%)	497 (10.0%)	527 (9.7%)
Hospital referral area‡ ∗						
Finnmark (N)	85	257	342	1 (1.2%)	9 (3.5%)	10 (2.9%)
UNN (N)	310	740	1 050	10 (3.2%)	41 (5.5%)	51 (4.9%)
Nordland (N)	225	574	799	6 (2.7%)	35 (6.1%)	41 (5.1%)
Helgeland (N)	148	346	494	10 (6.8%)	17 (4.9%)	27 (5.5%)
Nord-Trøndelag (C)	191	458	649	9 (4.7%)	30 (6.6%)	39 (6.0%)
St. Olavs (C)	400	1 051	1 451	16 (4.0%)	112 (10.7%)	128 (8.8%)
Møre-Romsdal (C)	342	861	1 203	18 (5.3%)	71 (8.2%)	89 (7.4%)
Førde (W)	165	424	589	7 (4.2%)	20 (4.7%)	27 (4.6%)
Bergen (W)	532	1 355	1 887	31 (5.8%)	122 (9.0%)	153 (8.1%)
Fonna (W)	251	648	899	11 (4.4%)	42 (6.5%)	53 (5.9%)
Stavanger (W)	500	1 134	1 634	23 (4.6%)	80 (7.1%)	103 (6.3%)
Østfold (SE)	445	985	1 430	12 (2.7%)	50 (5.1%)	62 (4.3%)
Akershus (SE)	814	1 631	2 445	27 (3.3%)	92 (5.6%)	119 (4.9%)
OUS (SE)	362	814	1 176	14 (3.9%)	56 (6.9%)	70 (6.0%)
Lovisenberg (SE)	95	212	307	5 (5.3%)	13 (6.1%)	18 (5.9%)
Diakonhjemmet (SE)	179	435	614	6 (3.4%)	26 (6.0%)	32 (5.2%)
Innlandet (SE)	666	1 463	2 129	13 (2.0%)	60 (4.1%)	73 (3.4%)
Vestre Viken (SE)	869	1 838	2 707	40 (4.6%)	137 (7.5%)	177 (6.5%)
Vestfold (SE)	481	979	1 460	14 (2.9%)	41 (4.2%)	55 (3.8%)
Telemark (SE)	323	746	1 069	8 (2.5%)	40 (5.4%)	48 (4.5%)
Sørlandet (SE)	461	998	1 459	6 (1.3%)	45 (4.5%)	51 (3.5%)

† Event is ablation, death, emigration or end of study period. For ablation patients the event is ablation.
‡ At the time of diagnosis.
∗ The four regional health authorities: N - North, C - Central, W - West and SE - South-East.

Table B2: Multivariable Cox regression, separate by gender, 2008-2010. Hazard ratios (95% confidence interval), adjusted for follow-up time.

	Model 1 (HT)			Model 2 (RHA)	
	Female	Male		Female	Male
Education			**Education**		
Low	1.0 (ref)	1.0 (ref)	Low	1.0 (ref)	1.0 (ref)
Medium	1.13 (0.83 - 1.53)	1.33 (1.11 - 1.60)	Medium	1.12 (0.83 - 1.52)	1.34 (1.11 - 1.60)
High	1.45 (1.02 - 2.06)	1.62 (1.33 - 1.97)	High	1.48 (1.04 - 2.10)	1.65 (1.36 - 2.01)
Income			**Income**		
Low	1.0 (ref)	1.0 (ref)	Low	1.0 (ref)	1.0 (ref)
Medium	1.11 (0.84 - 1.46)	1.43 (1.18 - 1.74)	Medium	1.14 (0.86 - 1.49)	1.44 (1.19 - 1.75)
High	1.06 (0.68 - 1.65)	1.77 (1.44 - 2.18)	High	1.12 (0.72 - 1.74)	1.81 (1.48 - 2.23)
Follow-up time (years)			**Follow-up time (years)**		
1	1.0 (ref)	1.0 (ref)	1	1.0 (ref)	1.0 (ref)
2	0.95 (0.73 - 1.22)	0.93 (0.82 - 1.06)	2	0.94 (0.73 - 1.21)	0.93 (0.82 - 1.05)
3	0.55 (0.37 - 0.81)	0.61 (0.50 - 0.74)	3	0.54 (0.37 - 0.81)	0.61 (0.50 - 0.73)
Hospital referral area (HT)			**Regional referral area (RHA)**		
Finnmark (N)	0.22 (0.03 - 1.62)	0.57 (0.29 - 1.13)	North	1.22 (0.81 - 1.85)	1.07 (0.87 - 1.32)
UNN (N)	0.86 (0.43 - 1.73)	0.81 (0.57 - 1.15)	Central	1.49 (1.06 - 2.10)	1.79 (1.53 - 2.10)
Nordland (N)	0.67 (0.28 - 1.59)	1.00 (0.69 - 1.46)	West	1.51 (1.13 - 2.01)	1.43 (1.24 - 1.66)
Helgeland (N)	1.54 (0.76 - 3.10)	0.77 (0.47 - 1.29)	South-East	1.0 (ref)	1.0 (ref)
Nord-Trøndelag (C)	1.02 (0.49 - 2.12)	1.11 (0.75 - 1.65)			
St. Olavs (C)	0.93 (0.52 - 1.66)	1.54 (1.20 - 1.97)			
Møre-Romsdal (C)	1.17 (0.67 - 2.05)	1.33 (1.00 - 1.78)			
Førde (W)	1.05 (0.47 - 2.35)	0.79 (0.49 - 1.27)			
Bergen (W)	1.40 (0.88 - 2.25)	1.38 (1.08 - 1.76)			
Fonna (W)	0.96 (0.49 - 1.89)	0.99 (0.70 - 1.40)			
Stavanger (W)	0.81 (0.48 - 1.36)	0.98 (0.74 - 1.30)			
Østfold (SE)	0.64 (0.33 - 1.22)	0.72 (0.52 - 1.00)			
Akershus (SE)	0.75 (0.46 - 1.23)	0.80 (0.61 - 1.04)			
OUS (SE)	0.91 (0.49 - 1.67)	0.85 (0.62 - 1.16)			
Lovisenberg (SE)	1.07 (0.42 - 2.73)	0.77 (0.44 - 1.37)			
Diakonhjemmet (SE)	0.67 (0.28 - 1.58)	0.69 (0.45 - 1.05)			
Innlandet (SE)	0.47 (0.25 - 0.88)	0.67 (0.50 - 0.92)			
Vestre Viken (SE)	1.0 (ref)	1.0 (ref)			
Vestfold (SE)	0.66 (0.36 - 1.21)	0.59 (0.42 - 0.84)			
Telemark (SE)	0.57 (0.27 - 1.22)	0.75 (0.53 - 1.07)			
Sørlandet (SE)	0.29 (0.12 - 0.69)	0.68 (0.48 - 0.95)			

C: 2011-2017 - After capacity increase

Table C1: Characteristics of patients 2011-2017.

	Atrial fibrillation			Ablation (% proportion with ablation)		
	Female	Male	Total	Female	Male	Total
Number of patients	26 887	55 415	82 302	2 415 (9.0%)	6 935 (12.5%)	9 350 (11.4%)
Age group‡						
Under 50	2 372	5 411	7 783	392 (16.5%)	1 217 (22.5%)	1 609 (20.7%)
50-59	3 516	9 612	13 128	514 (14.6%)	2 052 (21.3%)	2 566 (19.5%)
60-69	10 386	23 003	33 389	1 095 (10.5%)	2 845 (12.4%)	3 940 (11.8%)
70 and older	10 613	17 389	28 002	414 (3.9%)	821 (4.7%)	1 235 (4.4%)
Education‡						
Low	7 668	12 152	19 820	494 (6.4%)	996 (8.2%)	1 490 (7.5%)
Medium	12 608	27 277	39 885	1 151 (9.1%)	3 223 (11.8%)	4 374 (11.0%)
High	6 611	15 986	22 597	770 (11.6%)	2 716 (17.0%)	3 486 (15.4%)
Income‡						
Low	12 454	8 909	21 363	845 (6.8%)	620 (7.0%)	1 465 (6.9%)
Medium	11 587	27 607	39 194	1 191 (10.3%)	2 986 (10.8%)	4 177 (10.7%)
High	2 846	18 899	21 745	379 (13.3%)	3 329 (17.6%)	3 708 (17.1%)
Hospital referral area‡ ∗						
Finnmark (N)	298	795	1 093	14 (4.7%)	59 (7.4%)	73 (6.7%)
UNN (N)	877	2 032	2 909	46 (5.2%)	205 (10.1%)	251 (8.6%)
Nordland (N)	688	1 595	2 283	29 (4.2%)	147 (9.2%)	176 (7.7%)
Helgeland (N)	478	1 015	1 493	33 (6.9%)	97 (9.6%)	130 (8.7%)
Nord-Trøndelag (C)	677	1 468	2 145	53 (7.8%)	191 (13.0%)	244 (11.4%)
St. Olavs (C)	1 260	2 962	4 222	192 (15.2%)	627 (21.2%)	819 (19.4%)
Møre-Romsdal (C)	1 151	2 585	3 736	141 (12.3%)	372 (14.4%)	513 (13.7%)
Førde (W)	525	1 240	1 765	37 (7.0%)	122 (9.8%)	159 (9.0%)
Bergen (W)	1 806	4 184	5 990	183 (10.1%)	624 (14.9%)	807 (13.5%)
Fonna (W)	856	1 958	2 814	103 (12.0%)	281 (14.4%)	384 (13.6%)
Stavanger (W)	3 173	4 920	8 093	160 (5.0%)	445 (9.0%)	605 (7.5%)
Østfold (SE)	1 557	3 165	4 722	126 (8.1%)	370 (11.7%)	496 (10.5%)
Akershus (SE)	2 568	4 897	7 465	219 (8.5%)	596 (12.2%)	815 (10.9%)
OUS (SE)	1 136	2 434	3 570	119 (10.5%)	344 (14.1%)	463 (13.0%)
Lovisenberg (SE)	342	739	1 081	41 (12.0%)	97 (13.1%)	138 (12.8%)
Diakonhjemmet (SE)	559	1 289	1 848	59 (10.6%)	203 (15.7%)	262 (14.2%)
Innlandet (SE)	2 296	4 638	6 934	161 (7.0%)	428 (9.2%)	589 (8.5%)
Vestre Viken (SE)	2 627	5 316	7 943	297 (11.3%)	705 (13.3%)	1 002 (12.6%)
Vestfold (SE)	1 421	2 792	4 213	127 (8.9%)	320 (11.5%)	447 (10.6%)
Telemark (SE)	1 019	2 156	3 175	118 (11.6%)	309 (14.3%)	427 (13.4%)
Sørlandet (SE)	1 573	3 235	4 808	157 (10.0%)	393 (12.1%)	550 (11.4%)

† Event is ablation, death, emigration or end of study period. For ablation patients the event is ablation.
‡ At the time of diagnosis.
∗ The four regional health authorities: N - North, C - Central, W - West and SE - South-East.

Table C2: Multivariable Cox regression, separate by gender, 2011-2017. Hazard ratios (95% confidence interval), adjusted for follow-up time.

	Model 1 (HT)			Model 2 (RHA)	
	Female	Male		Female	Male
Education			**Education**		
Low	1.0 (ref)	1.0 (ref)	Low	1.0 (ref)	1.0 (ref)
Medium	1.27 (1.14 - 1.41)	1.29 (1.20 - 1.39)	Medium	1.28 (1.15 - 1.42)	1.31 (1.21 - 1.40)
High	1.29 (1.14 - 1.47)	1.66 (1.54 - 1.80)	High	1.32 (1.17 - 1.49)	1.71 (1.58 - 1.84)
Income			**Income**		
Low	1.0 (ref)	1.0 (ref)	Low	1.0 (ref)	1.0 (ref)
Medium	1.21 (1.10 - 1.33)	1.49 (1.36 - 1.62)	Medium	1.21 (1.10 - 1.33)	1.49 (1.36 - 1.62)
High	1.34 (1.17 - 1.54)	1.71 (1.57 - 1.88)	High	1.32 (1.15 - 1.51)	1.70 (1.55 - 1.86)
Follow-up time (years)			**Follow-up time (years)**		
1	1.0 (ref)	1.0 (ref)	1	1.0 (ref)	1.0 (ref)
2	0.58 (0.53 - 0.65)	0.69 (0.65 - 0.73)	2	0.58 (0.52 - 0.64)	0.68 (0.65 - 0.73)
3	0.46 (0.40 - 0.52)	0.45 (0.42 - 0.49)	3	0.45 (0.40 - 0.51)	0.45 (0.42 - 0.49)
4	0.40 (0.34 - 0.47)	0.41 (0.37 - 0.45)	4	0.39 (0.34 - 0.46)	0.41 (0.37 - 0.45)
5	0.52 (0.44 - 0.62)	0.39 (0.35 - 0.43)	5	0.52 (0.44 - 0.61)	0.38 (0.34 - 0.43)
6	0.50 (0.40 - 0.62)	0.46 (0.41 - 0.53)	6	0.50 (0.40 - 0.62)	0.46 (0.41 - 0.53)
7	0.35 (0.24 - 0.50)	0.34 (0.27 - 0.42)	7	0.35 (0.24 - 0.50)	0.34 (0.27 - 0.42)
Hospital referral area (HT)			**Regional referral area (RHA)**		
Finnmark (N)	0.42 (0.24 - 0.72)	0.61 (0.47 - 0.79)	North	0.55 (0.46 - 0.66)	0.80 (0.73 - 0.87)
UNN (N)	0.49 (0.36 - 0.66)	0.83 (0.71 - 0.97)	Central	1.40 (1.25 - 1.57)	1.52 (1.42 - 1.62)
Nordland (N)	0.41 (0.28 - 0.60)	0.78 (0.65 - 0.93)	West	0.69 (0.62 - 0.77)	0.93 (0.87 - 0.99)
Helgeland (N)	0.58 (0.40 - 0.83)	0.80 (0.65 - 0.99)	South-East	1.0 (ref)	1.0 (ref)
Nord-Trøndelag (C)	0.74 (0.56 - 1.00)	1.14 (0.97 - 1.34)			
St. Olavs (C)	1.55 (1.29 - 1.86)	1.86 (1.67 - 2.07)			
Møre-Romsdal (C)	1.17 (0.96 - 1.43)	1.24 (1.09 - 1.41)			
Førde (W)	0.68 (0.48 - 0.96)	0.84 (0.69 - 1.02)			
Bergen (W)	0.98 (0.81 - 1.17)	1.21 (1.08 - 1.34)			
Fonna (W)	1.20 (0.96 - 1.50)	1.27 (1.10 - 1.46)			
Stavanger (W)	0.31 (0.26 - 0.38)	0.60 (0.53 - 0.67)			
Østfold (SE)	0.81 (0.66 - 1.00)	0.99 (0.87 - 1.13)			
Akershus (SE)	0.78 (0.65 - 0.93)	0.98 (0.87 - 1.09)			
OUS (SE)	0.92 (0.74 - 1.14)	1.01 (0.89 - 1.15)			
Lovisenberg (SE)	0.98 (0.71 - 1.36)	0.92 (0.75 - 1.14)			
Diakonhjemmet (SE)	0.91 (0.68 - 1.20)	1.06 (0.91 - 1.25)			
Innlandet (SE)	0.67 (0.56 - 0.82)	0.80 (0.71 - 0.91)			
Vestre Viken (SE)	1.0 (ref)	1.0 (ref)			
Vestfold (SE)	0.79 (0.64 - 0.98)	0.91 (0.80 - 1.04)			
Telemark (SE)	1.12 (0.90 - 1.38)	1.19 (1.04 - 1.36)			
Sørlandet (SE)	0.95 (0.79 - 1.16)	1.00 (0.88 - 1.13)			

D: 2013-2017 - Fibrillation only

Table D1: Characteristics of patients 2013-2017.

	Atrial fibrillation			Ablation (% proportion with ablation)		
	Female	Male	Total	Female	Male	Total
Number of patients	19 619	42 341	61 960	1 543 (7.9%)	4 604 (10.9%)	6 147 (9.9%)
Age group‡						
Under 50	1 046	3 548	4 594	157 (15.0%)	697 (19.6%)	854 (18.6%)
50-59	2 373	6 930	9 303	309 (13.0%)	1 260 (18.2%)	1 569 (16.9%)
60-69	7 675	17 460	25 135	724 (9.4%)	1 983 (11.4%)	2 707 (10.8%)
70 and older	8 525	14 403	22 928	353 (4.1%)	664 (4.6%)	1 017 (4.4%)
Education‡						
Low	5 491	9 002	14 493	326 (5.9%)	630 (7.0%)	956 (6.6%)
Medium	9 338	20 816	30 154	743 (8.0%)	2 144 (10.3%)	2 887 (9.6%)
High	4 790	12 523	17 313	474 (9.9%)	1 830 (14.6%)	2 304 (13.3%)
Income‡						
Low	8 885	6 343	15 228	544 (6.1%)	365 (5.8%)	909 (6.0%)
Medium	8 642	21 178	29 820	746 (8.6%)	1 928 (9.1%)	2 674 (9.0%)
High	2 092	14 820	16 912	253 (12.1%)	2 311 (15.6%)	2 564 (15.2%)
Hospital referral area‡ ∗						
Finnmark (N)	229	616	845	7 (3.1%)	42 (6.8%)	49 (5.8%)
UNN (N)	728	1 664	2 392	31 (4.3%)	136 (8.2%)	167 (7.0%)
Nordland (N)	575	1 310	1 885	21 (3.7%)	105 (8.0%)	126 (6.7%)
Helgeland (N)	385	793	1 178	23 (6.0%)	62 (7.8%)	85 (7.2%)
Nord-Trøndelag (C)	516	1 133	1 649	41 (7.9%)	142 (12.5%)	183 (11.1%)
St. Olavs (C)	941	2 269	3 210	153 (16.3%)	457 (20.1%)	610 (19.0%)
Møre-Romsdal (C)	883	1 998	2 881	110 (12.5%)	277 (13.9%)	387 (13.4%)
Førde (W)	432	1 004	1 436	28 (6.5%)	87 (8.7%)	115 (8.0%)
Bergen (W)	1 471	3 375	4 846	133 (9.0%)	434 (12.9%)	567 (11.7%)
Fonna (W)	655	1 457	2 112	75 (11.5%)	183 (12.6%)	258 (12.2%)
Stavanger (W)	1 259	2 693	3 952	81 (6.4%)	260 (9.7%)	341 (8.6%)
Østfold (SE)	1 115	2 310	3 425	85 (7.6%)	239 (10.3%)	324 (9.5%)
Akershus (SE)	2 025	3 856	5 881	141 (7.0%)	372 (9.6%)	513 (8.7%)
OUS (SE)	862	1 899	2 761	73 (8.5%)	225 (11.8%)	298 (10.8%)
Lovisenberg (SE)	286	646	932	22 (7.7%)	67 (10.4%)	89 (9.5%)
Diakonhjemmet (SE)	418	1 014	1 432	31 (7.4%)	148 (14.6%)	179 (12.5%)
Innlandet (SE)	1 800	3 660	5 460	98 (5.4%)	270 (7.4%)	368 (6.7%)
Vestre Viken (SE)	2 009	4 189	6 198	154 (7.7%)	421 (10.1%)	575 (9.3%)
Vestfold (SE)	1 026	2 103	3 129	75 (7.3%)	198 (9.4%)	273 (8.7%)
Telemark (SE)	733	1 655	2 388	65 (8.9%)	207 (12.5%)	272 (11.4%)
Sørlandet (SE)	1 271	2 697	3 968	96 (7.6%)	272 (10.1%)	368 (9.3%)

† Event is ablation, death, emigration or end of study period. For ablation patients the event is ablation.
‡ At the time of diagnosis.
∗ The four regional health authorities: N - North, C - Central, W - West and SE - South-East.

Table D2: Multivariable Cox regression, separate by gender, 2013-2017. Hazard ratios (95% confidence interval), adjusted for follow-up time.

	Model 1 (HT)			Model 2 (RHA)	
	Female	Male		Female	Male
Education			**Education**		
Low	1.0 (ref)	1.0 (ref)	Low	1.0 (ref)	1.0 (ref)
Medium	1.22 (1.07 - 1.40)	1.30 (1.19 - 1.42)	Medium	1.23 (1.08 - 1.41)	1.31 (1.20 - 1.43)
High	1.25 (1.07 - 1.46)	1.66 (1.51 - 1.83)	High	1.27 (1.08 - 1.48)	1.70 (1.54 - 1.87)
Income			**Income**		
Low	1.0 (ref)	1.0 (ref)	Low	1.0 (ref)	1.0 (ref)
Medium	1.16 (1.03 - 1.30)	1.52 (1.36 - 1.71)	Medium	1.16 (1.03 - 1.30)	1.53 (1.37 - 1.71)
High	1.35 (1.13 - 1.60)	1.81 (1.61 - 2.03)	High	1.33 (1.12 - 1.58)	1.82 (1.62 - 2.05)
Follow-up time (years)			**Follow-up time (years)**		
1	1.0 (ref)	1.0 (ref)	1	1.0 (ref)	1.0 (ref)
2	0.63 (0.55 - 0.71)	0.63 (0.59 - 0.68)	2	0.62 (0.55 - 0.71)	0.63 (0.59 - 0.68)
3	0.48 (0.41 - 0.56)	0.42 (0.38 - 0.46)	3	0.47 (0.41 - 0.55)	0.41 (0.38 - 0.46)
4	0.39 (0.32 - 0.47)	0.35 (0.31 - 0.39)	4	0.38 (0.31 - 0.47)	0.34 (0.31 - 0.39)
5	0.21 (0.14 - 0.30)	0.21 (0.17 - 0.26)	5	0.21 (0.14 - 0.30)	0.21 (0.17 - 0.26)
Hospital referral area (HT)			**Regional referral area (RHA)**		
Finnmark (N)	0.39 (0.18 - 0.83)	0.76 (0.55 - 1.04)	North	0.59 (0.47 - 0.73)	0.83 (0.74 - 0.93)
UNN (N)	0.59 (0.40 - 0.86)	0.89 (0.73 - 1.07)	Central	1.87 (1.64 - 2.14)	1.77 (1.64 - 1.91)
Nordland (N)	0.51 (0.32 - 0.81)	0.89 (0.72 - 1.11)	West	1.12 (0.98 - 1.27)	1.12 (1.04 - 1.20)
Helgeland (N)	0.71 (0.46 - 1.10)	0.85 (0.65 - 1.11)	South-East	1.0 (ref)	1.0 (ref)
Nord-Trøndelag (C)	1.08 (0.77 - 1.53)	1.41 (1.17 - 1.71)			
St. Olavs (C)	2.37 (1.89 - 2.96)	2.30 (2.02 - 2.63)			
Møre-Romsdal (C)	1.72 (1.34 - 2.19)	1.57 (1.35 - 1.83)			
Førde (W)	0.91 (0.61 - 1.36)	0.96 (0.76 - 1.21)			
Bergen (W)	1.24 (0.99 - 1.57)	1.32 (1.16 - 1.51)			
Fonna (W)	1.69 (1.28 - 2.23)	1.42 (1.19 - 1.69)			
Stavanger (W)	0.74 (0.56 - 0.96)	0.93 (0.80 - 1.08)			
Østfold (SE)	1.09 (0.84 - 1.42)	1.12 (0.96 - 1.32)			
Akershus (SE)	0.91 (0.72 - 1.14)	0.99 (0.87 - 1.14)			
OUS (SE)	1.10 (0.83 - 1.45)	1.15 (0.98 - 1.36)			
Lovisenberg (SE)	0.91 (0.58 - 1.43)	0.94 (0.72 - 1.22)			
Diakonhjemmet (SE)	0.93 (0.63 - 1.37)	1.33 (1.10 - 1.60)			
Innlandet (SE)	0.75 (0.58 - 0.96)	0.84 (0.72 - 0.98)			
Vestre Viken (SE)	1.0 (ref)	1.0 (ref)			
Vestfold (SE)	1.00 (0.76 - 1.31)	1.00 (0.84 - 1.18)			
Telemark (SE)	1.23 (0.92 - 1.64)	1.35 (1.14 - 1.59)			
Sørlandet (SE)	1.05 (0.81 - 1.35)	1.06 (0.91 - 1.24)