Less educated and older patients have reduced access to biologic DMARDs even in a country with highly developed social welfare (Norway): results from Norwegian cohort study NOR-DMARD

Polina Putrik¹,², Sofia Ramiro³, Elisabeth Lie⁴, Andras P. Keszei⁵, Tore K. Kvien⁴, Désirée van der Heijde³,⁴, Robert Landewe⁶,⁷, Till Uhlig⁴,⁸,* and Annelies Boonen¹,*

Abstract

Objective. To explore whether age, gender or education influence the time until initiation of the first bDMARD in patients with RA.

Methods. Data from the Norwegian Register of DMARDs collected between 2000 and 2012 were used. Only DMARD-naïve patients with RA starting their first conventional synthetic DMARD were included in the analyses. The start of the first bDMARD was the main outcome of interest. Cox regression analyses were used to explore the impact of education, age and gender on the start of a first bDMARD, adjusting for confounders, either at baseline or varying over time (time-varying model).

Results. Of 1946 eligible patients [mean (s.d.) age: 55 (14) years, 68% females], 368 (19%) received a bDMARD during follow-up (mean 2.6 years). In the baseline prediction model, older age [Hazard Ratio (HR) 0.97, 95% CI: 0.96, 0.98], lower education [HR = 0.76 and 0.68 for low and intermediate education levels vs college/university education, respectively (P = 0.01)] and female gender [only in the period 2000–2003, HR = 0.61 (95% CI: 0.41, 0.91)] were associated with a lower hazard ratio to start a bDMARD. The time-varying model provided overall consistent results, but the effect of education was only relevant for older patients (>57 years) and became more pronounced by the end of the decade.

Conclusions. Less educated and older patients have disadvantages with regard to access to costly treatments, even in a country with highly developed welfare like Norway. Females had lower access in the beginning of the 2000s, but access had improved by the end of the decade.

Key words: rheumatic diseases, epidemiology, biological therapies, health policies, attitude of health professionals

Rheumatology key messages

- Poorly educated and older patients with RA have less access to bDMARDs in Norway.
- Disadvantage in access to bDMARDs for less educated and older RA patients increased over last decade.

¹Rheumatology, Maastricht University Medical Center and CAPHRI Research Institute Maastricht University, ²Health Promotion and Education, Maastricht University, Maastricht, ³Rheumatology, Leiden University Medical Center, Leiden, the Netherlands, ⁴Rheumatology, Diakonhjemmet Hospital, Oslo, Norway, ⁵Medical Informatics, Uniklinik RWTH Aachen University, Aachen, Germany, ⁶Amsterdam Rheumatology & Immunology Center, Amsterdam, Amsterdam, ⁷Rheumatology, Atrium Medical Center, Heerlen, the Netherlands and ⁸Rheumatology, Diakonhjemmet Hospital, National Advisory Unit on Rehabilitation in Rheumatology, Oslo, Norway

Submitted 17 August 2015; revised version accepted 16 February 2016

*Till Uhlig and Annelies Boonen contributed equally to this study.

Correspondence to: Polina Putrik, Department of Health Promotion, Maastricht University, Debyeplein 1, Maastricht 6229HA, the Netherlands. E-mail: polina.putrik@gmail.com
Introduction

Persisting inequalities in health are alarming, and available evidence suggests that in recent years the gap in health for disadvantaged groups has even increased [1–3]. While inequality is a general term used to refer to differences in health, inequity is an ethical term that emphasizes the avoidable and unjust character of some of the existing inequalities [4–6]. Individual factors across which inequities may occur have been summarized across socio-economic, demographic or geographic factors in terms of Place of Residence, Race/Ethnicity, Occupation, Gender, Religion, Education, Socio-economic Status and Social Capital, and the Plus (PROGRESS-Plus framework) represents additional categories such as Age, Disability, Sexual Orientation and Literacy [5, 7–9]. This framework represents a systematic way of approaching factors over which the individual has little or no control, and to which stakeholders should pay particular attention in an attempt to address eventual inequities. There are numerous reasons why disparities may exist across these factors. The WHO brings together a number of individual and system factors that can influence and determine health outcomes [10]. Among these, access and utilization of health-care services, recognized as independent determinants of health, are particularly relevant for patients living with chronic conditions.

In RA, a chronic autoimmune rheumatic disease that can result in extensive joint destruction, research into inequities and into access to care is scarce. The development of biologic DMARDs (bDMARDs) has advanced the treatment of RA. These drugs, however, are very costly, and 1 year of treatment with a biologic drug in Europe is over 50 times more expensive than a treatment with a conventional synthetic DMARD (csDMARD) [11]. The position of bDMARDs in the treatment strategies for RA is a continuing field of research and point of discussion in the development of national and international treatment recommendations [12]. Similarly, health-care decision-makers regulate access to these reimbursed drugs in almost all European countries. Available evidence reveals that such regulations on access to biologics on a national and regional level result in differential access to drugs, with lower access in countries or regions with lower socio-economic welfare [11, 13–17]. However, professional and national/regional guidelines regulating access are based on clinical criteria and never on personal, demographic or socio-economic factors.

Notwithstanding, gradients in access to treatment with bDMARDs, however, have also been described across individual socio-economic or PROGRESS factors. A recent study by Yelin et al. [18] in the USA showed that, at the individual level, younger age and higher socio-economic status measured by income were associated with earlier access to biologic DMARDs, independent of disease characteristics. Another study in the USA has also pointed to a high level of heterogeneity in the initiation of a treatment with csDMARDs or bDMARDs by age, income, postal code area or health insurance plan [19]. Evidence from Europe on individual socio-economic factors in relation to access to these treatments is scarce, and only one Swedish study reported that for women with RA, treatment with anti-TNF therapy (the first class of bDMARDs that was available) was initiated at a higher level of subjective disease activity than for men, but at the same level of physician-reported disease activity [20]. No evidence with respect to other PROGRESS factors in relation to access to bDMARDs in RA is available. Data on access to treatment across groups at risk for being disadvantaged will provide relevant information for rheumatologists and health-care decision-makers in continuing attempts to improve equity of access and ultimately health of all patients.

The objective of the current study was to explore whether there are differences in initiation rates for a first bDMARD in patients with RA across age, gender and educational level in a prosperous country with a health-care system based on solidarity and universal access to reimbursed health care (Norway).

Materials and patients

Study design and data collection

Data from the Norwegian Register of DMARDs (NOR-DMARD) were used. NOR-DMARD is a register of patients with inflammatory joint diseases treated with DMARDs, both csDMARDs and bDMARDs. Five rheumatology departments covering approximately one third of the total population provided patient data from 2000 onwards [21]. Each time a new DMARD was started, study variables were collected at initiation, after 3, 6 and 12 months and then yearly up to treatment termination. In February 2013, NOR-DMARD comprised 6839 treatment courses in a total of 4126 patients with confirmed RA.

The cohort selected for these analyses included DMARD-naïve patients starting treatment with their first csDMARD and without previous treatment with a bDMARD. Patients with <1 year of follow-up (entered into the cohort in 2012 or later) were excluded from the longitudinal analyses.

The NOR-DMARD has been approved by the Norwegian Data Inspectorate and the Regional Ethics Committee of Eastern Norway. Patients gave written informed consent before inclusion [22]. This study did not require additional ethical approval.

Study variables

The main outcome of interest was the time till start of a first bDMARD. Data on age, gender, education, comorbidities, RF, erosive disease, date for fulfilment of ACR criteria for RA, and previous and current csDMARD therapy were collected at the first visit of each new treatment course. Tender joint count and swollen joint count, patient global assessment, ESR, Modified Stanford HAQ (a validated and commonly used self-report measure to assess physical function) and physician global assessment on a 100-mm visual analogue scale were collected at all visits. For each visit, the DAS28, the measure of disease activity universally used to follow the course of RA and treatment...
target, was calculated from the tender joint count, swollen joint count, ESR and patient global assessment (visual analogue scale) [23].

Education was originally recorded in seven categories and for the purpose of the analyses further grouped into low education (7 years of primary school or shorter; 9 years of primary school; middle school/junior high school), intermediate education (1–2 years of high school; high school degree) and high education (college or university, <4 years; college or university, ≥4 years). Disease duration (time since the diagnosis) was dichotomized into <1 year or ≥1 year. Year of entrance into the cohort was categorized into three strata (2000-03, 2004-08 and 2009-11).

The Rheumatic Disease Comorbidity Index was calculated from the Medical Dictionary for Regulatory Activities classification that was used in NOR-DMARD to record comorbidities. For this purpose, an algorithm was developed to reclassify diseases of Medical Dictionary for Regulatory Activities into the disease groups contained within the Rheumatic Disease Comorbidity Index, namely pulmonary disorders, myocardial infarction, other cardiovascular disorders, stroke, hypertension, diabetess, spine/hip/leg fracture, depression, gastro-ulcer, other gastro-disorders and cancer [24, 25].

Statistical analysis

We modelled the predictors of the start of a first bDMARD using Cox proportional hazard regression analysis. Socio-economic factors (age, gender and education) were the variables of interest, and potential confounders included DAS28, Modified Stanford HAQ, RF, erosive disease (present vs not), disease duration and comorbidities. To explore whether the influence of socio-economic status on time until start of a first bDMARD would change over time, year of entry of the patients into the register (three strata) was included. All factors of interest and potential confounders were first explored in univariable Cox regression analysis, and those variables that were statistically significant in the univariable model (at P < 0.10) were entered in a multivariable model using manual forward selection (at P < 0.05). Multivariable models always included education, age, gender and comorbidities. In the first model, predictors and potential confounders were modelled at baseline (model I), while in the second model, a time-varying model, potential confounders were allowed to vary at each available visit until the moment of event (model II) [26]. Adjusted failure curves based on estimates derived from the final Cox regression model were built.

Mutual pairwise interactions between education, age and gender, as well as between these factors and DAS28 and year of entrance into the cohort were investigated, and stratification was performed when the P-values for the interaction term was <0.10.

Analyses were done in complete cases. Additionally, missing values were imputed using multiple imputation with chained equations. Five imputation datasets were generated, and parameter estimates were combined using Rubin’s rule [27, 28]. Analyses were repeated on imputed data and results were compared. Statistical software Stata 12 was used [29].

Results

In total, 1946 DMARD-naive patients with a total of 3037 treatment courses during the observation time were included in the cohort (supplementary Fig. S1, available at Rheumatology Online). The average observation time per patient was 3.4 (SD 2.8) years. At baseline, patients had a mean (s.d.) age of 55 (14) years, and nearly two-thirds were female (68%) (Table 1). About one-third of patients were assigned to the low-education group (n = 629, 33%), one-third to the intermediate-education group (n = 685, 35%) and the remaining third were college/university graduates (high-education group) (n = 607, 32%). Mean (s.d.) DAS28 at baseline was 4.8 (1.4). Nearly one-third of patients had one or more comorbidities at baseline (n = 703, 27%) (Table 1). In general, the percentage of missing data was low (supplementary Table S1, available at Rheumatology Online).

Almost 19% (n = 368) of patients were prescribed at least one bDMARD during the observation time. Fourteen per cent of low-, 17% of intermediate- and 26% of high-education patients started on a bDMARD, and the mean (s.d.) DAS28 at commencement was 5.3 (1.4), 5.1 (1.4) and 4.5 (1.5), respectively (Fig. 1). On average, patients were prescribed a biologic 2.6 (s.d. 2.2) years after entering the cohort (Table 1).

In the model using baseline variables only (Table 2 and Fig. 2), older age and lower level of education for low and intermediate education vs high, respectively) resulted in a lower likelihood of starting a first bDMARD. In addition, a higher DAS28 and HAQ at baseline, as well as positivity for RF resulted in a higher likelihood, while the number of comorbidities was not contributory. The effect of gender was different across calendar years (interaction P = 0.01), and stratified analyses revealed that while in the first years of the decade (2000-03) female gender was associated with a lower hazard of starting a bDMARD, the gender effect was reversed at the end of the decade (2009-11). Other interactions in the model with baseline variables were either not statistically significant or not clinically meaningful after stratification.

The time-varying model (Table 3), accounting for changes in clinical predictors over time, confirmed that older age but also female gender were associated with a lower likelihood of starting a first bDMARD. Among clinical variables, the presence of erosive disease and a higher DAS28 were significant predictors of the start of a bDMARD. A significant interaction between education and age was present (P = 0.09), and stratified analyses by median age (i.e. 57 years old) showed that lower education was only associated with a lower likelihood of starting a bDMARD in older patients. The effect of low education on time-to-first bDMARD prescription was only significant in those patients in the 2009-11 stratum compared with those who entered before 2003.
Table 1 Demographic and clinical characteristics of the 1946 patients with RA

<table>
<thead>
<tr>
<th>Variable</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at baseline, mean (s.d.), years</td>
<td>55.4 (14.0)</td>
</tr>
<tr>
<td>Gender, female, n (%)</td>
<td>1319 (68)</td>
</tr>
<tr>
<td>Education at baseline</td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>629 (33)</td>
</tr>
<tr>
<td>Intermediate</td>
<td>685 (35)</td>
</tr>
<tr>
<td>High (college/university)</td>
<td>607 (32)</td>
</tr>
<tr>
<td>DAS28 at baseline, mean (s.d.)</td>
<td>4.8 (1.4)</td>
</tr>
<tr>
<td>Disease duration &lt;1 year at baseline, n (%)</td>
<td>1593 (84)</td>
</tr>
<tr>
<td>HAQ at baseline (0–3), mean (s.d.)</td>
<td>0.6 (0.5)</td>
</tr>
<tr>
<td>Pain VAS at baseline (0–100), mean (s.d.)</td>
<td>45.0 (24.6)</td>
</tr>
<tr>
<td>RF, n (%)</td>
<td>1121 (59)</td>
</tr>
<tr>
<td>Erosive disease, n (%)</td>
<td>498 (27)</td>
</tr>
<tr>
<td>Rheumatic disease Comorbidity Index, mean (s.d.)</td>
<td>0.6 (0.5)</td>
</tr>
<tr>
<td>Rheumatic disease Comorbidity Index ≥1 at baseline, n (%)</td>
<td>703 (27)</td>
</tr>
<tr>
<td>Received a biologic during observation time, n (%)</td>
<td>368 (19)</td>
</tr>
<tr>
<td>Mean time to first biologic, years, mean (s.d.)</td>
<td>2.6 (2.2)</td>
</tr>
<tr>
<td>Year of entry into cohort, n (%)</td>
<td></td>
</tr>
<tr>
<td>2000–03</td>
<td>542 (28)</td>
</tr>
<tr>
<td>2004–08</td>
<td>810 (41)</td>
</tr>
<tr>
<td>2009–11</td>
<td>594 (31)</td>
</tr>
</tbody>
</table>

VAS: Visual Analogue Scale.

(Interaction P = 0.08) (in 2009–11, HR was 0.26, 95% CI: 0.12, 0.58) and 0.70 (95% CI: 0.40, 1.20) for low and intermediate education vs high, respectively. All other interactions were either not statistically significant or not clinically relevant after stratification.

Sensitivity analyses with imputed data confirmed the results of the main analysis based on non-imputed data (data not shown).

Discussion

This study explored differences in time to start a first bDMARD across three individual socio-economic factors (age, gender and educational status) in patients with RA in Norway. Older patients and those with less education had a lower likelihood of starting a bDMARD over time, after careful adjustment for those factors that were expected to determine the initiation of a biologic, such as disease severity and disease activity. In addition, females had lower access when bDMARDs became initially available in the period 2000–03, but they caught-up and the situation had completely reversed by the end of the decade. When accounting for variation in disease activity and severity over time, older and female patients had worse access, and patients with the lowest level of education had a clear disadvantage at an older age (>57), and in most recent years (2009–11). In conclusion, even in a prosperous country, access to costly treatment is not only influenced by clinical factors (according to existing treatment recommendations [12]), but also by factors such as gender, age and level of education.

The Norwegian health-care system is characterized by universal access to high-quality medical services for all citizens at reasonable expenditure levels. With regard to reimbursed access to bDMARDs, Norway was among the countries with one of the most liberal regulations on access in Europe, with respect to number of biologics reimbursed as well as clinical requirements for prescription [11, 17]. In addition, a recent analysis within NOR-DMARD reported that overall prescription rates of bDMARDs in RA and other diseases have increased steadily over time, and the disease activity at which the biologic is prescribed has, as expected, become lower and achieved better treatment results [30, 31].

Paradoxically, the current study revealed that in later years 2008–11 (compared with 2000–03), less educated patients had an even stronger disadvantage in access to bDMARDs compared with highly educated patients. Thus, while overall these drugs have become more widely prescribed, not all patients have equally benefited from this change. It could be that advances in medical technologies may actually increase the health gap across socio-economic determinants because persons belonging to higher socio-economic status groups may have better resources (material or immaterial) and benefit more from the new and more efficacious technologies.

With regard to gender, it has been reported previously that females with symptoms of RA not only were referred later to medical specialists than men, in Norway [32–34], but also showed worse response to treatment with DMARDs [34]. Arkema et al. [20] has showed that in Swedish women with RA, treatment with anti-TNF therapy was initiated at a higher level of subjective disease activity than in men, although levels of physician-reported disease activity were similar, suggesting that patient-perceived disease activity is not taken into consideration when making the treatment decision. A recent paper by Austad et al. [35] reported that in the Oslo Rheumatoid Arthritis Register, females showed larger improvements in patient-reported outcomes than men. Our results consistently showed that while in the early 2000s there was a delay in the start of a bDMARD in females compared with males at the same level of disease activity, this situation changed over the decade, and by the years 2009–11 females appeared to have even better access to these treatments than men. This observation could reflect the general development in the Norwegian society over the last 2–3 decades, with disappearing gender differences regarding work and household activities. It is possible that female patients communicate better their RA-related limitations and needs for further improvement of the disease activity. Qualitative research will be informative to shed light on gender differences in uptake of biologic drugs.
Notably, inequalities in the prescription of bDMARDs by age have persisted over years. These inequalities could neither be explained by a higher number of comorbidities in older patients that could be a contra-indication for biologic therapy, nor by a lower RA disease activity. Furthermore, the older patients with lower education were even further disproportionally disadvantaged in terms of access to bDMARDs, which may indicate that these patients comprise a particularly vulnerable group. Similar findings on inequalities in access to biologics by age or socio-economic status have been recently reported in the USA [18].

**TABLE 2** Predictors of treatment with bDMARDs, adjusted for confounders at baseline (model I)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hazard ratio (95% CI)</th>
<th>Stratified by year of entry into cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total sample, n = 1565</td>
<td>2000-03, n = 480</td>
</tr>
<tr>
<td>Gender (female vs male)</td>
<td>0.99 (0.78, 1.27)</td>
<td>0.61 (0.41, 0.91)</td>
</tr>
<tr>
<td>Age at baseline, years</td>
<td>0.97 (0.96, 0.98)</td>
<td>0.96 (0.95, 0.98)</td>
</tr>
<tr>
<td>Education at baseline:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High education (ref. category)</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Intermediate education</td>
<td>0.68 (0.53, 0.88) b</td>
<td>0.74 (0.47, 1.17)</td>
</tr>
<tr>
<td>Low education</td>
<td>0.76 (0.56, 1.03) b</td>
<td>1.29 (0.76, 2.20)</td>
</tr>
<tr>
<td>DAS28 at baseline</td>
<td>1.20 (1.09, 1.33)</td>
<td>1.03 (0.86, 1.22)</td>
</tr>
<tr>
<td>HAQ at baseline (0-3)</td>
<td>1.44 (1.11, 1.86)</td>
<td>1.72 (1.10, 2.69)</td>
</tr>
<tr>
<td>RF (yes vs no)</td>
<td>1.29 (1.02, 1.63)</td>
<td>1.81 (1.21, 2.71)</td>
</tr>
<tr>
<td>Year of entry into the cohort</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2000–03 (reference category)</td>
<td>1.00</td>
<td>—</td>
</tr>
<tr>
<td>2004–08 vs 2000–03</td>
<td>1.46 (1.11, 1.92)</td>
<td>—</td>
</tr>
<tr>
<td>2009–11 vs 2000–03</td>
<td>3.11 (2.22, 4.35)</td>
<td>—</td>
</tr>
<tr>
<td>Rheumatic disease</td>
<td>0.93 (0.81, 1.07)</td>
<td>0.86 (0.66, 1.11)</td>
</tr>
</tbody>
</table>

aEstimates are derived from a multivariable model. bOverall P-value for education (two dummy variables) = 0.01.
On reflection about potential explanations of inequalities in the uptake of expensive biologics in a country like Norway, with universal access to health care, it is not so much the availability (e.g. presence on the market) or affordability (e.g. price and reimbursement policies) of these medications, but rather the acceptability component of access, e.g. cultural and subjective perceptions and behaviors of patients (often referred to as health literacy) and physicians. More educated and younger patients may have better information and may have superior negotiation capabilities when discussing treatment options with their physicians. For example, Barton et al. [36] showed that older RA patients in California who were fluent in English, but had low health literacy, communicated suboptimally with their doctors. At the same time, physicians may unconsciously consider judgments beyond clinical factors in their decisional process, such as risk for adverse events, risk for non-adherence to treatment and safety warnings, and need for maintenance of diverse social roles and responsibilities.

This study has several limitations. First, only a limited number of individual socio-economic determinants were examined. Second, the study population was restricted to patients with early RA. Third, the study was conducted in a single country with universal access to health care, which may not be generalizable to other settings. Fourth, the study did not consider the role of patient preferences and decisional capacity.

On reflection about potential explanations of inequalities in the uptake of expensive biologics in a country like Norway, with universal access to health care, it is not so much the availability (e.g. presence on the market) or affordability (e.g. price and reimbursement policies) of these medications, but rather the acceptability component of access, e.g. cultural and subjective perceptions and behaviors of patients (often referred to as health literacy) and physicians. More educated and younger patients may have better information and may have superior negotiation capabilities when discussing treatment options with their physicians. For example, Barton et al. [36] showed that older RA patients in California who were fluent in English, but had low health literacy, communicated suboptimally with their doctors. At the same time, physicians may unconsciously consider judgments beyond clinical factors in their decisional process, such as risk for adverse events, risk for non-adherence to treatment and safety warnings, and need for maintenance of diverse social roles and responsibilities.

This study has several limitations. First, only a limited number of individual socio-economic determinants were examined. Second, the study population was restricted to patients with early RA. Third, the study was conducted in a single country with universal access to health care, which may not be generalizable to other settings. Fourth, the study did not consider the role of patient preferences and decisional capacity.

On reflection about potential explanations of inequalities in the uptake of expensive biologics in a country like Norway, with universal access to health care, it is not so much the availability (e.g. presence on the market) or affordability (e.g. price and reimbursement policies) of these medications, but rather the acceptability component of access, e.g. cultural and subjective perceptions and behaviors of patients (often referred to as health literacy) and physicians. More educated and younger patients may have better information and may have superior negotiation capabilities when discussing treatment options with their physicians. For example, Barton et al. [36] showed that older RA patients in California who were fluent in English, but had low health literacy, communicated suboptimally with their doctors. At the same time, physicians may unconsciously consider judgments beyond clinical factors in their decisional process, such as risk for adverse events, risk for non-adherence to treatment and safety warnings, and need for maintenance of diverse social roles and responsibilities.

This study has several limitations. First, only a limited number of individual socio-economic determinants were examined. Second, the study population was restricted to patients with early RA. Third, the study was conducted in a single country with universal access to health care, which may not be generalizable to other settings. Fourth, the study did not consider the role of patient preferences and decisional capacity.

On reflection about potential explanations of inequalities in the uptake of expensive biologics in a country like Norway, with universal access to health care, it is not so much the availability (e.g. presence on the market) or affordability (e.g. price and reimbursement policies) of these medications, but rather the acceptability component of access, e.g. cultural and subjective perceptions and behaviors of patients (often referred to as health literacy) and physicians. More educated and younger patients may have better information and may have superior negotiation capabilities when discussing treatment options with their physicians. For example, Barton et al. [36] showed that older RA patients in California who were fluent in English, but had low health literacy, communicated suboptimally with their doctors. At the same time, physicians may unconsciously consider judgments beyond clinical factors in their decisional process, such as risk for adverse events, risk for non-adherence to treatment and safety warnings, and need for maintenance of diverse social roles and responsibilities.

This study has several limitations. First, only a limited number of individual socio-economic determinants were examined. Second, the study population was restricted to patients with early RA. Third, the study was conducted in a single country with universal access to health care, which may not be generalizable to other settings. Fourth, the study did not consider the role of patient preferences and decisional capacity.

On reflection about potential explanations of inequalities in the uptake of expensive biologics in a country like Norway, with universal access to health care, it is not so much the availability (e.g. presence on the market) or affordability (e.g. price and reimbursement policies) of these medications, but rather the acceptability component of access, e.g. cultural and subjective perceptions and behaviors of patients (often referred to as health literacy) and physicians. More educated and younger patients may have better information and may have superior negotiation capabilities when discussing treatment options with their physicians. For example, Barton et al. [36] showed that older RA patients in California who were fluent in English, but had low health literacy, communicated suboptimally with their doctors. At the same time, physicians may unconsciously consider judgments beyond clinical factors in their decisional process, such as risk for adverse events, risk for non-adherence to treatment and safety warnings, and need for maintenance of diverse social roles and responsibilities.

This study has several limitations. First, only a limited number of individual socio-economic determinants were examined. Second, the study population was restricted to patients with early RA. Third, the study was conducted in a single country with universal access to health care, which may not be generalizable to other settings. Fourth, the study did not consider the role of patient preferences and decisional capacity.
available for analysis, and factors like occupation, income, place of residence and origin were not recorded. Further, we did not possess data that would allow us to further explain the relation between education and access (e.g. health literacy of patients). An important question remaining for the future research agenda is whether earlier access to treatment by younger male patients with high socio-economic status results in better disease outcomes compared with patients with disadvantaged socio-economic status. However, as all recommendations for the treatment of RA underlie the treat-to-target principle that aims at lowest possible disease activity [12], it should be considered unfair that for similar levels of disease activity and similar levels of comorbidities, the uptake of innovative but expensive medications is subject to age and gender diversity and determined by socio-economic position. Further studies should attempt to better understand factors impacting the clinical decision-making process with regards to RA treatment.

In conclusion, we have found that poorly educated and older patients have potentially decisive disadvantages with regard to access to expensive treatments, even in a prosperous country with universal access to health care like Norway. While gender diversity seems to have become less relevant over time, the disadvantage for the elderly persists, and the disadvantage for the less educated seems to have even increased over time, especially in the elderly. Our findings should alert the healthcare professionals and other stakeholders to join efforts in order to reduce health inequities.

Acknowledgements

Data collection was supported by the Eastern Norway Regional Health Authority. The Norwegian Disease-Modifying Antirheumatic Drug study has received unrestricted grant support from Abbott, Amgen, Wyeth, Aventis, MSD, Schering-Plough/Centocor, Bristol-Myers Squibb, Roche and the Norwegian Directorate for Health and Social Affairs. Contributorship statement: A.B. conceived the idea for this manuscript, P.P., S.R. and A.B. received the idea for this manuscript, P.P., S.R. and A.B. contributed to interpretation of the results, and T.K.K., Dv.H., A.P.K. provided the statistical and methodological support. P.P., S.R., E.L., A.P.K., T.K.K., Dy.H., R.L., T.U. and A.B. contributed to interpretation of the results, editing of the manuscript and read and approved the final version.

Funding: No specific funding was received from any bodies in the public, commercial or not-for-profit sectors to carry out the work described in this manuscript.

Disclosure statement: A.B. received research grants to her department from Amgen, Abbvie, Pfizer and Merck, and receives occasional honoraria from Sandoz, Janssen and Pfizer. R.L. has acted as a consultant for Abbott/AbbVie, Abylnx, Amgen, Astra-Zeneca, Bristol-Myers Squibb, Celgene, Janssen (formerly Centocor), Galapagos, Glaxo-Smith-Kline, Novartis, Novo-Nordisk, Merck, Pfizer, Roche, Schering-Plough, TiGenix, UCB, Wyeth. A.B. has also received research grants from Abbott, Amgen, Centocor, Novartis, Pfizer, Roche, Schering-Plough, UCB, Wyeth and speaker fees from Abbott/AbbVie, Amgen, Bristol Myers Squibb, Janssen (formerly Centocor), Merck, Pfizer, Roche, Schering-Plough, UCB, Wyeth. R.L. is also director of Rheumatology Consultancy BV, which is a registered company under Dutch law. All other authors have declared no conflicts of interest.

Supplementary data

Supplementary data are available at Rheumatology Online.

References


16 Hoebert JM, Mantel-Teeuwisse AK, van Dijk L, Bijlsma JW, Leufkens HG. Do rheumatoid arthritis patients have equal access to treatment with new medicines?: Tumour necrosis factor-alpha inhibitors use in four European countries. Health Policy 2012;104:76–83.


29 StataCorp. Stata Statistical Software: Release 12. College Station, TX: StataCorp LP, 2011.


