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Research paper

Sociodemographic factors and uncomplicated cystitis in women aged 15–50 years: a nationwide Swedish cohort registry study (1997–2018)

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ABSTRACT

Background: Symptoms suggestive of uncomplicated cystitis constitutes one of the most common reasons to seek health care in otherwise healthy women. Previous studies regarding the relationship between sociodemographic factors and uncomplicated cystitis are limited, mainly because of the lack of nationwide population-based data from primary healthcare settings, where most uncomplicated cystitis are diagnosed.

Methods: A Swedish nation-wide open cohort study consisting of 2 044 065 females who were 15–50 years of age during the study period (1997–2018) was conducted. The outcome was first event uncomplicated cystitis diagnosed in primary health care rather than an assessment of the "true" incidence, which is not feasible in nationwide datasets. Cox regression models were used in the statistical analyses.

Findings: The study identified 546 076 first events of uncomplicated cystitis (26•7% of the study population), corresponding to an incidence rate per 100 person-years of 2•91 (95% CI 2•90–2•91). In fully adjusted models, rural living was associated with lower risks of uncomplicated cystitis (Hazard ratio, HR, 0•67; 95% CI, 0•66–0•68) compared to urban living, while both Middle Eastern/North African (HR, 1•15; 95% CI, 1•14–1•16) and Latin American/Caribbean (HR, 1•24; 95% CI, 1•22–1•27) women had higher risks compared to Swedish women. Low education and low income were also associated with higher risks compared to high education and high income.

Interpretation: This study presents novel risk factors associated with uncomplicated cystitis in women. The findings may help health care workers in the treatment of women with symptoms of uncomplicated cystitis.

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1. Introduction

Uncomplicated cystitis, also known as uncomplicated lower urinary tract infection (UTI), is one of the most common bacterial infection in otherwise healthy women. The annual incidence proportion is about 10% and up to 60% of all females experience uncomplicated UTI at least once during their lifetime [1–3].

Well-known risk factors for uncomplicated cystitis are previous episodes, family history of cystitis, frequent and recent intercourse, a new sex partner, and use of a diaphragm with spermicide; these risk factors have been linked to both increased incidence and recurrency of uncomplicated cystitis [1,4–6]. Low socioeconomic status (SES) is another potential risk factor that has recently been suggested for UTI

in Bangladesh [7], where it was found that young female garment workers have an increased risk of UTI. These findings suggest that younger women of lower socioeconomic status generally have higher risks of UTI. Another study from the same country found that self-reported financial distress may be a result of UTI [8].

Many developing countries do not have equal health care access, which may lead to socioeconomic health inequalities, including disparities in the diagnosis and treatment of UTIs. It is unknown, however, whether these disparities also exist in countries that has universal tax-financed health care services with the goal to provide health care on equal terms for the entire population [9], irrespective of individual income, country of birth and urban/rural living. This gap in previous research is most likely due to the lack of nationwide population-based datasets from primary healthcare, where commonly diagnosed infections, such as UTI, most often are treated. Sweden is an ideal setting to investigate if sociodemographic inequalities for UTI or, more specifically, the commonly occurring uncomplicated cystitis, exist in a country with universal health care. This is because

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Research in context

Evidence before this study

Uncomplicated lower urinary tract infection (UTI), also known as uncomplicated cystitis, is one of the most common bacterial infection in otherwise healthy females. The infection is primarily diagnosed and treated in primary health care settings. While sociodemographic differences in health are well-known it is to our knowledge yet to be studied for uncomplicated cystitis. We searched PubMed in August 2020 for uncomplicated cystitis, cystitis, UTI, risk factors and sociodemographic factors. While one study from Bangladesh suggested low socioeconomic status to be a risk factor for UTI in women, another study from the UK described a higher rate of UTI in women from the higher social classes. However, no studies were identified that had investigated the relationship between a comprehensive set of sociodemographic factors and uncomplicated cystitis in women with access to universal health care, especially not on a nationwide basis. This is likely due to the previous lack of nationwide population-based data from primary healthcare settings.

Added value of this study

Using population-based primary healthcare data in Sweden we identified that low socioeconomic status (i.e., low income and low education) and being born in certain regions outside of Sweden (i.e., Middle East/North Africa and Latin America/the Caribbean) were independently associated with a higher risk of uncomplicated cystitis. Living outside of the major cities was linked to a lower risk of uncomplicated cystitis compared to urban living.

Implications of all the available evidence

Uncomplicated cystitis is a very common infection in primary healthcare amongst women. This study presents novel risk factors associated with first event uncomplicated cystitis and that sociodemographic inequalities associated with uncomplicated cystitis in women exist. The findings could spare many women from misdiagnosis and overdiagnosis with potentially unnecessary antibiotic therapies and thus minimize the antibiotic use in the society, as well as decrease the costs for the patients and the entire healthcare system. Future studies to investigate possible mechanisms explaining the associations are warranted.

2.2. Ascertainment of outcome variable

The first incident of uncomplicated cystitis during the study period was identified in the Swedish Primary Health Care Register from 1997 and onwards until the end of 2018. The coverage of the data varied over time and region. The time periods are different depending on the time before digitalizing the patient records in a certain region. In 2015, the register contained 72% of the population living in Sweden[10] and at the end of the present study, 87% of the population was included. Cystitis is classified with the code N30 according to the 10th revision of the *International Classification of Diseases* [11]. We did not consider subtypes of cystitis that were not classified as acute infective cystitis (i.e., N301, N302, N303, N304, and N308). We excluded women with pregnancy or comorbidities not aligned with the diagnosis uncomplicated cystitis[1,12–14] as follows: (A) Ongoing pregnancy at the time of the cystitis event (National Medical Birth Register); (B) History of HIV, immunodeficiency disorder, or diabetes mellitus, defined as any such diagnosis (ICD-10: B20–24, D80–89, E10–11) within two years prior to the cystitis event (Primary Healthcare Register, Out Patient Register and Hospital Discharge Register); (C) History of non-male urological neoplasms (ICD-10: C64–68, D41), or paraplegic syndrome, chronic nephritic syndrome, hereditary nephropathy, chronic pyelonephritis, hydronephrosis, nephropathy, other serious kidney diseases, kidney failure, urolithiasis, neurological bladder dysfunction, congenital or other diseases of kidney, bladder or urinary tract, defined as any such diagnosis (ICD-10: M623, N03, N07, N11, N13–23, N25–29, N32, Q60–64) within two years prior to the cystitis event (Primary Healthcare Register, Out Patient Register and Hospital Discharge Register); and (D) History of redeemed prescription on anti-neoplastic and/or immunomodulating agents (ATC code: L) or corticosteroids for systemic use (ATC code: H02) within six months prior to the cystitis event (Prescription Register).

2.3. Predictor variables

All variables were measured at baseline/inclusion. *Age groups* were defined as 15–24, 25–34, 35–44, and 45–50 years of age. Individual socioeconomic status was defined by educational level and family income. *Educational level* was classified into three categories according to the duration of school attendance: (i) compulsory schooling or less (≤ 9 years); (ii) short or partial high school education (10–11 years); (iii) completed high school education or more, such as university or college education (≥ 12 years). For those aged 15–17 years (included in the youngest age group, i.e., 15–24 years) the parents' (highest) educational level was used. The reason for using parental educational level in the age 15–17 years is because they did not have a chance to finish their education and become more independent from their parents before inclusion. *Family income* was calculated as annual family income divided by the number of members in the family. The income calculation was weighted, taking the ages of the family members into account. For example, children were given lower consumption weights than adults. The calculation was performed as follows: the sum of all family members' incomes was multiplied by the individual's consumption weight divided by the family members' total consumption weight. The final variable was calculated as empirical quartiles from the distribution and classified into four groups: low, middle-low, middle-high, and high. *Region of residence* was divided into three groups: large cities, Southern Sweden, and Northern Sweden. *Country of birth* was defined as being born in any of the following countries/regions: Sweden; Eastern European countries; Western countries; Middle East/North Africa; Africa (excluding North Africa); Asia (excluding Middle East) and Oceania; or Latin America and the Caribbean. The choice of these categories was based on countries with geographical proximity and/or cultural and economic similarities. Middle Eastern countries were

Sweden has nationwide health care datasets linked to population data at the individual level.

With this study we aimed to investigate whether there is a relationship between socioeconomic factors (education and income), region of residency, and country of birth and the risk of uncomplicated cystitis in women aged 15–50 years diagnosed in primary healthcare.

2. Methods

2.1. Study design and setting

The study was designed as an open cohort study. The study population consisted of 2 044 065 females aged 15–50 years during the study period from January 1, 1997 to December 31, 2018. The first event of uncomplicated cystitis during the study period was defined as outcome variable. Each woman could only be included once. This research was conducted at the Center for Primary Health Care Research at Lund University in Malmö, Sweden.

combined with countries in North Africa, i.e., MENA. However, we did not include countries included in the Greater Middle East, such as Afghanistan and Pakistan. Those countries were defined as Asian countries, excluding the Middle East. Eastern European countries included countries in the former Soviet Bloc and Western countries included European countries (excluding Eastern Europe) and Australia, New Zealand, Canada and USA.

2.4. Data sources

Registers used in this study were (time period when the data was available to us is shown in brackets): Swedish Primary Healthcare Register (1997–2018), which includes nationwide clinical diagnoses from primary healthcare consultations in Sweden; Medical Birth Register (1997–2015), which includes data on, e.g., pregnancies in Sweden; Hospital Discharge Register (1997–2015) and Out Patient Register (2001–2015), which include hospital discharge diagnoses and diagnoses from outpatient specialist care, respectively; Prescription Register (2005–2015), which contain the specific ATC codes on redeemed medical drug prescriptions; and Cause of Death Register (1997–2015). The Total Population Register was used to collect data on emigration, country of birth, income, education, and other socio-demographic data. The population registers are nearly 100% complete for the entire national population [15]. All linkages between the individual-level clinical and population registry data were performed using a pseudonymized version of the unique 10-digit personal identification number assigned to each person in Sweden for her lifetime.

2.5. Statistical analysis

Descriptive statistics, i.e., number of events and population sizes, were calculated in each category of the different variables. Person-years were calculated from the start of follow-up on 1 January 1997 until the first event of uncomplicated cystitis, death, emigration, or closing date on 31 December 2018. Incidence rates (per 100 person-years) were calculated for each category of the different variables for the whole follow-up period. Cox regression models were used to estimate Hazard ratios (HR) and 95% confidence intervals (CI) to test for the association between the predictor variables and time to first event of uncomplicated cystitis during the study period. The time-period started on January 1, 1997 and proceeded until first event of uncomplicated cystitis, or death, emigration, or end of the study period on December 31, 2018. Three models were used, where Model 1 was a univariate model for each variable; Model 2 was adjusted for age; and Model 3 was adjusted for age and the other covariates listed above. The proportionality assumptions were checked by plotting the incidence rates over time and by calculating Schoenfeld (partial) residuals and these assumptions were fulfilled. This means that the strength of the associations did not change over time. We did not exclude observations with missing values (range 0•0% – 4•6%). For education and income, they were instead included in the groups with the lowest levels of education and income, respectively. Unknown region of residence (1%) was included in the category large cities. Unknown country of birth (in total 188 individuals, 0%) was included in the category “born in Sweden”. SAS software version 9.4 [16] was used for all statistical analyses. A two-tailed p-value of <0•05 was used for statistical significance in the main outcomes.

2.6. Ethical consideration

This study was approved by the Regional Ethical Review Board in Lund (Dnr 2012/795 [6/2 2013]).

2.7. Role of the funding source

The funding sources of the study had no role in the study design; in the collection, analysis, and interpretation of data; or in the writing of the report, nor in the decision to submit the paper for publication. All authors confirm that they had full access to all the data in the study and accept responsibility to submit for publication.

3. Results

The study population consisted of 2 044 065 women aged 15–50 years during the study period 1997–2018. The number of first event uncomplicated cystitis events during the study period was 546 076 (26•7% of the study population), corresponding to an incidence per 100 person-years of 2•91 (95% CI 2•90–2•91).

Table 1 describes the characteristics of the study population and distribution of the number of first events of uncomplicated cystitis by age, educational level, family income, region of residence and country of birth. Of the first events of uncomplicated cystitis, 34•1% occurred in the youngest age group (aged 15–24 years), which comprised 28•6% of the study population, and 69•3% occurred in women living in large cities, which corresponded to 62•6% of the study population. Missing data varied between 0•0% and 4•6% (data not shown in table).

Table 2 shows that the incidence rate per 100 person-years of first event uncomplicated cystitis was particularly high in the youngest age group (aged 15–24 years), i.e., 3•82 (95% CI 3•80–3•83). The incidence rates were also high in the lowest educated and lowest income group. The larger cities had a higher incidence rate of 3•13 (95% CI 3•12–3•14) compared to 2•11 (95% CI 2•09–2•13) in Northern Sweden. For country of birth, the incidence rates were highest among women from the Middle East/North Africa and Latin America/the Caribbean. Their incidence rates were 3•94 (95% CI 3•90–3•98) and 3•99 (3•91–4•07), respectively.

Table 3 presents the associations between the individual sociodemographic variables and first event uncomplicated cystitis. In model 1, the univariate analysis showed that young age, low education, low family income, living in larger cities, or being born in the Middle East/North Africa or Latin America/the Caribbean were associated with a higher risk of first event uncomplicated cystitis compared to their corresponding reference. For example, being a female aged 15–24 years, yielded a HR of 1•45 (95% CI 1•43–1•46) of being diagnosed with a first event uncomplicated cystitis, compared to the oldest age group. In model 2, the age-adjusted model yielded similar results for the variable country of birth, but the results for the socioeconomic variables were somewhat attenuated. For example, the higher HR of first event uncomplicated cystitis amongst women from the Middle East/North Africa compared to women from Sweden remained significant at a HR of 1•25 (95% CI 1•24–1•26). In model 3, adjusting for all covariates, most of the significant results for the socioeconomic variables remained but were further attenuated. The HRs for the variable region of residence remained almost unchanged in all models, with lower HRs of first event uncomplicated cystitis in women not living in large cities. For example, the HR was 0•67 (95% CI 0•66–0•68) for women living in Northern Sweden. The Middle Eastern/North African women had a HR of 1•15 (95% CI 1•14–1•16) compared to women from Sweden when adjusting for all the other covariates. The corresponding HR for women from Latin America/the Caribbean was 1•24 (95% CI 1•22–1•27).

We performed interaction tests between the two socioeconomic variables (education, income) and country of birth but found no meaningful statistical interactions. We also performed an additional analysis where we adjusted for parity (categorized as 1 child, 2 children, 3 children, 4 children and 5 or more children). Parity was also analysed in a continuous manner. Although parity was associated

Table 1

Characteristics of study population and number of first events of uncomplicated cystitis in women aged 15–50 years old during the study period 1997–2018.

	Total population of women 15–50 years of age		No. of first events of uncomplicated cystitis	
	No.	%	No.	%
Age groups (years)				
15–24	584 389	28•6	186 253	34•1
25–34	589 188	28•8	149 367	27•4
35–44	554 795	27•1	133 966	24•5
45–50	315 693	15•4	76 490	14•0
Educational level				
≤ 9	328 936	16•1	99 042	18•1
10–11	423 741	20•7	121 163	22•2
≥ 12	1 291 388	63•2	325 871	59•7
Family income				
Low	510 155	25•0	145 272	26•6
Middle-low	510 580	25•0	146 942	26•9
Middle-high	512 299	25•0	137 334	25•1
High	511 031	25•0	116 528	21•3
Region of residence				
Large cities	1 279 428	62•6	378 610	69•3
Southern Sweden	518 887	25•4	117 181	21•5
Northern Sweden	245 750	12•0	50 285	9•2
Country of birth				
Sweden	1 563 956	76•5	423 024	77•5
Eastern Europe	115 994	5•7	28 841	5•3
Western countries	97 918	4•8	22 346	4•1
Middle East/North Africa	115 640	5•7	34 266	6•3
Africa (excluding North Africa)	43 068	2•1	10 211	1•9
Asia (excluding Middle East) and Oceania	78 167	3•8	17 990	3•3
Latin America and the Caribbean	29 322	1•4	9398	1•7
All	2 044 065	100•0	546 076	100•0

with uncomplicated cystitis, it did not affect the main results, so we chose not to include parity in the main analysis.

4. Discussion

The main findings indicate that the sociodemographic factors young age, low education, low family income, living in a large city,

Table 2
Incidence rate (per 100 person-years) of first event uncomplicated cystitis in women aged 15–50 years old during the study period 1997–2018.

	Incidence rate (IR) per 100 person-years		
	IR	95% CI	
Age groups (years)			
15–24	3•82	3•80	3•83
25–34	2•75	2•74	2•77
35–44	2•48	2•47	2•49
45–50	2•50	2•49	2•52
Educational level			
≤ 9	3•48	3•45	3•50
10–11	2•80	2•79	2•82
≥ 12	2•81	2•80	2•82
Family income			
Low	3•38	3•36	3•40
Middle-low	2•87	2•85	2•88
Middle-high	2•79	2•77	2•80
High	2•64	2•63	2•66
Region of residence			
Large cities	3•13	3•12	3•14
Southern Sweden	2•74	2•72	2•75
Northern Sweden	2•11	2•09	2•13
Country of birth			
Sweden	2•81	2•80	2•82
Eastern Europe	3•03	3•00	3•07
Western countries	2•99	2•95	3•03
Middle East/North Africa	3•94	3•90	3•98
Africa (excluding North Africa)	3•32	3•25	3•38
Asia (excluding Middle East) and Oceania	2•97	2•92	3•01
Latin America and the Caribbean	3•99	3•91	4•07
All	2•91	2•90	2•92

and being born in the Middle East/North Africa or Latin America/the Caribbean are all independently associated with increased risks of being diagnosed with first event uncomplicated cystitis. Although this study does not examine possible mechanisms behind the increased risk of uncomplicated cystitis in regard to the investigated sociodemographic exposures, the findings are suggestive of an unequal distribution of this illness among women aged 15–50 years.

In this nation-wide cohort of 2 044 065 women, 26•7% had at least one event of uncomplicated cystitis during the study period, and of these a little over one third were in the youngest age group (aged 15–24 years). A similar pattern of a particularly high incidence of similar magnitude in the young otherwise healthy female population has generally been observed in previous studies [2–4]. The consistency between our results and those from previous studies supports that our data sources are representative and that it is likely that we can identify most UTIs in the database.

Women of lower socioeconomic status (measured as lower education and lower income) were found to have a higher risk of uncomplicated cystitis in our cohort. To our knowledge, no other studies have used population data on socioeconomic status to examine the relation with uncomplicated cystitis. Butler et al. [3], used a population-based survey that included self-reported data and described a higher rate of at least one UTI amongst women in the higher social classes in UK but otherwise there is a lack of more extensive analyses in previous literature. The findings from UK are in contrast to our findings, which might be explained by our larger sample size, different data sources or the different methods of measuring both the predictor variables and the outcome (i.e., recall survey vs. registry data, and at least one UTI vs. first event of uncomplicated cystitis). It is possible that our findings could be explained by campaigns leading to a lower use of antibiotics in Sweden compared to the UK [17]. For example, in a recent recommendation for uncomplicated cystitis from 2017, the Swedish Medical Product Agency recommended watchful-waiting (including increased fluid intake) if the symptoms are not considered severe for the patient [18]. It is possible that women of higher socioeconomic status are more educated in regard to self-treatment for mild cystitis symptoms and therefore “better” at following

Table 3

Association of individual sociodemographic status and first event uncomplicated cystitis in women aged 15–50 years old during the study period 1997–2018; Hazard Ratios (HR), 95% Confidence Intervals (95% CI) and P-values are presented for each model.

Covariates	Model 1			P-value	Model 2			P-value	Model 3			
	HR	95% CI			HR	95% CI			HR	95% CI	P-value	
Age (ref. age 45–50 years)												
15–24	1•45	1•43	1•46	<•0001	1•45	1•43	1•46	<•0001	1•41	1•40	1•42	<•0001
25–34	1•09	1•08	1•10	<•0001	1•09	1•08	1•10	<•0001	1•08	1•07	1•09	<•0001
35–44	1•00	0•99	1•01	0•370	1•00	0•99	1•01	0•370	0•98	0•97	0•99	<•0001
Educational level (ref. ≥ 12 years)												
≤ 9	1•24	1•23	1•25	<•0001	1•18	1•17	1•19	<•0001	1•14	1•14	1•15	<•0001
10–11	1•06	1•06	1•07	<•0001	1•12	1•11	1•13	<•0001	1•12	1•11	1•13	<•0001
Family income (ref. High)												
Low	1•30	1•29	1•31	<•0001	1•17	1•16	1•18	<•0001	1•12	1•11	1•13	<•0001
Middle-low	1•19	1•18	1•19	<•0001	1•13	1•12	1•14	<•0001	1•12	1•11	1•13	<•0001
Middle-high	1•12	1•11	1•13	<•0001	1•09	1•08	1•10	<•0001	1•08	1•07	1•09	<•0001
Region of residence (ref. Large cities)												
Southern Sweden	0•81	0•81	0•82	<•0001	0•80	0•79	0•80	<•0001	0•80	0•79	0•80	<•0001
Northern Sweden	0•68	0•68	0•69	<•0001	0•67	0•67	0•68	<•0001	0•67	0•66	0•68	<•0001
Country of birth (ref. Sweden)												
Eastern Europe	1•00	0•98	1•01	0•5017	1•02	1•01	1•03	0•0003	0•96	0•95	0•97	<•0001
Western countries	0•97	0•96	0•99	0•0001	1•04	1•03	1•06	<•0001	1•00	0•99	1•02	0•6067
Middle East/North Africa	1•25	1•24	1•26	<•0001	1•25	1•24	1•26	<•0001	1•15	1•14	1•16	<•0001
Africa (excluding North Africa)	1•02	1•00	1•04	0•0864	1•00	0•99	1•02	0•6574	0•93	0•91	0•94	<•0001
Asia (excluding Middle East) and Oceania	0•95	0•94	0•96	<•0001	0•98	0•96	0•99	0•0023	0•91	0•89	0•92	<•0001
Latin America and the Caribbean	1•31	1•28	1•34	<•0001	1•34	1•31	1•37	<•0001	1•24	1•22	1•27	<•0001

Model 1: Univariate model; Model 2: age adjusted model; Model 3: Fully adjusted model.

recommendations. However, it is also possible that Swedish women with higher SES are more likely to obtain a correct diagnosis of symptoms suggestive of cystitis.

Region of residency was strongly associated with the risk of uncomplicated cystitis and remained unchanged after full adjustments. There were significantly lower risks of first event uncomplicated cystitis occurring outside the larger cities in both Northern and Southern Sweden. Since uncomplicated cystitis could be regarded as self-limited in over one in four patients treated with placebo, without a clinically relevant risk difference for severe complications (e.g., pyelonephritis) compared to those treated with antibiotics [19–21], our findings were not unexpected. It is plausible that women in more rural regions, with longer geographic distance to healthcare, would wait longer to seek healthcare. Thus, they would be more prone to self-treatment without a medical diagnosis being registered for a possible cystitis event. It has been noted by Butler et al. [3], that 5% of women with UTI symptoms do not seem to visit a physician, and it is possible that this proportion is higher in women with longer geographic distance to healthcare. Another plausible explanation to why urban living was found to be associated with a higher risk of uncomplicated cystitis in our study could be that women living in urban areas in Sweden have more sexual partners [22], and new sexual partners is a well-known risk factor for UTI [5].

Women born in the Middle East/North Africa or Latin America/the Caribbean had a higher risk for uncomplicated cystitis compared to Swedish-born women, especially before the adjustments for the other covariates. When adjusting for the socioeconomic factors and region of residency, the increased risks of first event uncomplicated cystitis were somewhat reduced in these women. This could be explained by the fact that a high proportion of immigrant women live in large cities and under poor socioeconomic circumstances. However, even when adjusting for the other covariates there was a 15% and 24% higher risk of being diagnosed with uncomplicated cystitis among women born in the Middle East/North Africa (HR, 1•15; 95% CI 1•14–1•16) and Latin America and the Caribbean (HR, 1•24; 95% CI 1•22–1•27), respectively. Although urban minorities have been linked to earlier sexual initiation in other countries [23], and sexual intercourse is a well-known risk factor for uncomplicated cystitis [4–

6], it is unlikely that our findings can be attributed only to that possible explanation; rather, it is more likely that multiple explanations exist. One possible explanation for the increased risk in Middle Eastern/North African and Latin American/Caribbean women may be misdiagnosis due to various reasons, as there are several other illnesses that presents themselves with similar symptoms [12,13]. Therefore, language barriers may possibly play a role.

It is important to diagnose UTI correctly in order to avoid unnecessary use of antibiotics, which may be harmful for both the individual and the society. Symptoms suggestive of uncomplicated cystitis constitute one of the most common reasons for women to seek health care and the infection can be diagnosed from symptoms alone, with a high diagnostic probability if done correctly [1,12,13]. When patients are misdiagnosed there is a risk of harming the patients if an unnecessary and potentially harmful treatment is given. A diagnosis of UTI has often been linked to antibiotic treatment in Sweden, with a 59–74% prescription rate [24,25], similar to findings in the UK [3]. In addition, antibiotics for UTI remains in general a leading cause of prescribed antibiotics in primary healthcare in Sweden [26].

However, the successful Swedish strategic program against antibiotic resistance (called “Strama” in Swedish, which means “rigorous” or “firm”) is constantly working closely with prescribers at the local level to monitor antibiotic use and inform about diagnosis and treatment of common bacterial infections, in order to reduce unnecessary prescribing of antibiotics for infections [27] such as uncomplicated cystitis. One necessary and important factor in this work is to treat all patients equally and be aware of potential cognitive biases [28] that might affect clinical decision making, including diagnosis and treatment decisions.

Although a physician should diagnose and treat all patients equally, this is not always the case as both individual physicians and the healthcare system as a whole are prone to both conscious and unconscious biases; therefore, sociodemographic healthcare inequalities may exist [29,30]. In Sweden, all tax-financed health care services are supposed to provide health care on equal terms for the entire population [9]. This study demonstrates, however, that sociodemographic inequalities associated with uncomplicated cystitis in women exist. This has also previously been shown in other recent studies in

Sweden that have demonstrated associations between socioeconomic status, country of birth and geographic region with risks of negative outcomes of various medical conditions [31–33], although these findings are not consistent [34].

The most important limitation with the present study is that it does not reflect the “true” incidence of uncomplicated cystitis, not including those patients that do not seek healthcare for this infection. However, our intention was to examine those cases of uncomplicated cystitis that were diagnosed in primary health care rather than assessing the “true” incidence, which is impossible in nationwide datasets. Although this potential bias is most likely non-differential it is possible that it might have varied somewhat between different groups with different health care seeking patterns (e.g., women living in urban vs. rural settings). There is also a possibility that we may have missed complicating factors (i.e., co-morbidities) although this is unlikely for most co-morbidities as we included other patient registers to assess complicating factors. Unfortunately, we did not have access to spoken language and it is possible that spoken language might have affected the results. However, the limitations in the study were balanced by the strengths. Major strengths with this study were that it involved several highly validated nation-wide data registries [15,35], which our research group is highly familiar with [31–34]. In addition, our group had access to primary health care data which is quite unique compared to most previous studies. Previous epidemiological studies on UTI [2–4] have mainly relied on surveys that may suffer from recall bias [2,3]. While previous epidemiological studies of different designs on UTI have involved at the most a couple of thousand patients, this nation-wide study population involves two million women with over half a million first events of uncomplicated cystitis during the study period, and an investigation of sociodemographic differences, which to the best of our knowledge not has been studied before, at least not on a nationwide basis.

Clinical implications of our findings for healthcare professionals are to pay more attention to potential sociodemographic differences, including country of birth, in female patients with symptoms suggestive of a cystitis, in order to improve the diagnosis and treatment of these patients. Furthermore, health care education to women with poor language skills about uncomplicated cystitis—symptoms, diagnosis (including differential diagnosis), natural course, and treatment options—could be considered from a public health perspective. This would be in line with the Swedish Strama’s education and awareness strategies [27] and could be incorporated in this and other similar programs, to minimize an unnecessary use of antibiotics.

In conclusion, our findings of increased risks of first event uncomplicated cystitis associated with socioeconomic status, country of birth, and urban living represent important information. These findings provide new knowledge on this common bacterial infection among otherwise healthy women. This could spare many women from misdiagnosis and overdiagnosis with potentially unnecessary antibiotic therapies and thus minimize the antibiotic use in the society, as well as decrease the costs for the patients and the entire healthcare system.

Contributors

All authors have approved the final version of the manuscript. Concept and development of idea: FJ and KS. Design: All authors. Access, acquisition, and analysis of data: KS and XL. Statistical analysis and tables: XL. Interpretation of data: All authors. Literature search and drafting of manuscript: FJ. Critical revision of the manuscript for intellectual content: KS and XL. The authors attest that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

Data availability statement

This study made use of several national registers and owing to ethical concerns, data cannot be made openly available. Further information regarding the health registries is available from the Swedish National Board of Health and Welfare: <https://www.socialstyrelsen.se/en/statistics-and-data/registers/> and Kristina Sundquist, co-author of this study and the one that holds the ethical permission for this study.

Declaration of interest

The authors have nothing to disclose.

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