Urolithiasis in immigrant groups

Scandinavian Journal of Urology

ISSN: 2168-1805 (Print) 2168-1813 (Online) Journal homepage: https://www.tandfonline.com/loi/isju20

Urolithiasis in immigrant groups: a nationwide cohort study in Sweden

Per Wändell, Axel C. Carlsson, Xinjun Li, Danijela Gasevic, Jan Sundquist & Kristina Sundquist

To cite this article: Per Wändell, Axel C. Carlsson, Xinjun Li, Danijela Gasevic, Jan Sundquist & Kristina Sundquist (2019): Urolithiasis in immigrant groups: a nationwide cohort study in Sweden, Scandinavian Journal of Urology, DOI: 10.1080/21681805.2019.1593241

To link to this article: https://doi.org/10.1080/21681805.2019.1593241

SCANDINAVIAN JOURNAL OF UROLOGY
https://doi.org/10.1080/21681805.2019.1593241

ARTICLE

OPEN ACCESS Check for updates

Urolithiasis in immigrant groups: a nationwide cohort study in Sweden

Per Wändell[a], Axel C. Carlsson[a], Xinjun Li[b], Danijela Gasevic[c,d], Jan Sundquist[b,e,f,g] and Kristina Sundquist[b,e,f,g]

[a]Division of Family Medicine and Primary Care, Department of Neurobiology, Care Sciences and Society, Karolinska Institutet, Huddinge, Sweden; [b]Center for Primary Health Care Research, Lund University, Malmö, Sweden; [c]Usher Institute of Population Health Sciences and Informatics, College of Medicine and Veterinary Medicine, University of Edinburgh, Edinburgh, UK; [d]School of Public Health and Preventive Medicine, Monash University, Melbourne, VIC, Australia; [e]Department of Family Medicine and Community Health, Icahn School of Medicine at Mount Sinai, New York, NY, USA; [f]Department of Population Health Science and Policy, Icahn School of Medicine at Mount Sinai, New York, NY, USA; [g]Department of Functional Pathology, Center for Community-based Healthcare Research and Education (CoHRE), School of Medicine, Shimane University, Matsue, Japan

ABSTRACT

Objective: To study the association between country of birth and incident urolithiasis in immigrant groups in Sweden, using individuals born in Sweden (or with Swedish-born parents in the second-generation study) as referents.

Methods: This nationwide follow-up study included first- and second-generation immigrants residing in Sweden between 1 January 1998 and 31 December 2012. Urolithiasis was defined as having at least one registered diagnosis of urolithiasis in the National Patient Register. Cox regression analysis was used to estimate the risk (hazard ratios (HR) with 95% confidence intervals (CI)) of incident urolithiasis. The models were stratified by sex and adjusted for age, sociodemographic status and co-morbidity.

Results: Compared to referents, slightly higher incidence rates and HRs of urolithiasis (HR; 95% CI) were observed among first-generation men (1.06; 1.04–1.09) and women (1.12; 1.08–1.16) but not among second-generation immigrants (persons born in Sweden with foreign-born parents). Among first-generation immigrants, higher HRs were noted among men and women from Central and Eastern Europe, Russia, Latin America, Africa and Asia. Lower HRs were seen among men and women from the Nordic countries, most Western European countries and North America. Among second-generation immigrants, higher HRs were noted among men and women from Denmark, Germany and Hungary, in men from Austria, and in women from the Netherlands and Poland. Lower HRs were seen in second generation immigrants from Latin America, Africa and Asia (men and women).

Conclusions: We observed substantial differences in incidence of urolithiasis between certain immigrant groups and the Swedish-born population, of importance in the clinical situation.

ARTICLE HISTORY
Received 16 January 2019
Accepted 7 March 2019

KEYWORDS
Urolithiasis; gender; first-generation immigrants; neighborhood; socioeconomic status

Introduction

Urolithiasis or urinary tract stone disease in most cases originates with stones formed in the kidney and leaves the body in the urine stream through the ureter, urine bladder and urethra [1,2]. While small stones can pass without any symptoms, stones of larger size, i.e. above 5 mm, may lead to severe stone colic cause through blockage in the ureter. Besides, urine bladder stones may also cause obstruction, but then of the urethra, also leading to problems with emptying the bladder.

Urolithiasis is a global problem. Historically, bladder stones have been known and treated since long ago, even if renal stones are more common nowadays [3]. However, the incidence and prevalence of kidney stones in particular are increasing globally [4], including in subgroups of sex, race, and age [5]. The figures of prevalence and incidence of urolithiasis in different regions and countries of the world do differ, with traditionally higher rates in the Western world [6], but there are large differences in the estimated levels even within countries, at least partly depending on methodological issues. Urolithiasis is more common among men than women [6,7], and background dietary risk factors for urolithiasis also differ by age and sex [6]. The global rise in especially kidney stones may be due to different factors [7], such as aging populations, changes in diet, and global warming [8], but also with higher registering of events owing to the use of more accurate diagnostic tools. In many non-Western countries, a shift to more Western diet habits seem to contribute to the changes [7], thus paralleling the increase in e.g. diabetes prevalence.

There are some studies of urolithiasis among immigrant groups in the Western world. A British study found immigrants from some countries with a known high incidence of urolithiasis retain their risk, such as immigrants from some

CONTACT Per Wändell per.wandell@ki.se Division of Family Medicine and Primary Care, Department of Neurobiology, Care Sciences and Society, Karolinska Institutet, Alfred Nobels Allé 23, Huddinge SE-141 83, Sweden

Supplemental data for this article can be accessed here.

East European countries, Turkey, and South Asia [9]. A study from New Zealand reported urolithiasis to be most frequent among individuals of Middle East origin, while immigrants from other Asian countries showed an incidence similar to that of individuals of European descent [10]. Some ethnic differences in risk for urolithiasis have also been described, especially in the US, with a higher risk among Caucasian populations and lower risk among African-Americans [6], but high also among Native Americans.

In Sweden, the number of immigrants has increased largely over the last decades, now reaching 17% for first-generation immigrants and, including second-generation immigrants, up to 25% [11].

The aim of this study was to explore the risk of being diagnosed with urolithiasis among first- and second-generation immigrants in Sweden and whether that risk differed from the Swedish-born reference population, after taking potential confounders into account.

Methods

Design

In the present study we used data from the National Patient Register, which includes diagnoses from in-hospital care, and from 2001 and onwards also from out-patient clinics, but not from primary health care. We also used data from the Total Population Register. We included subjects aged 45 years and older. The follow-up period ran from 1 January 1998 until hospitalisation/out-patient treatment of urolithiasis at an age of diagnosis of 45 years or more, death, emigration or the end of the study period on 31 December 2012, whichever came first.

Outcome variable

Upper urolithiasis: N20 (including N20.0 (calculus of kidney), N20.1 (calculus of ureter), N20.2 (calculus of kidney with calculus of ureter), N20.9 (urinary calculus, unspecified)).

N13.2 (hydronephrosis with renal and ureteral stone).

Lower urolithiasis: N21 (including N21.0 (calculus in bladder); N21.1 (calculus in urethra), N21.8 (other lower urinary tract calculus), N21.9 (calculus of lower urinary tract, unspecified)).

Urolithiasis in other diseases: N22.0 (urinary calculus in schistosomiasis).

N22.8 (calculus of urinary tract in other diseases classified elsewhere), E72.0 (cystinuria).

E74.8 (primary hyperoxaluria), and E79.8 (xanthine and 2,8–dihydroxyadenine stones).

Time was calculated from 1 January 1998 until hospitalisation/out-patient treatment of urolithiasis, and until 31 December 2012.

Co-morbidities

The following co-morbidities according to ICD-10 codes were identified: obesity (E65 and E66); diabetes mellitus (E10–E14); hyperlipidemia (E78.0, E78.1, E78.2, E78.3, E78.4, and E78.5); hypertension (I10–I15); coronary heart disease (I20–I25); gout (M10); ESRD (N18.5 (i.e. CKD stage 5), T82.4, Y84.1, Z49, Z94.0, and Z99.2 (ICD-10 codes for ESRD, dialysis or transplantation), and V9211, V9212, V9200, V9531, V9532, V9507, KAS00, KAS10, KAS20, KAS40, KAS50, KAS60, KAS96, KAS97, JAK10, TJA33, TJA35, and TKA20 (surgical codes for transplantation or dialysis)).

Demographic and socioeconomic variables

We stratified the study population by *sex*, as there sex differences in the urolithiasis risk [6].

Age was used as a continuous variable in the analysis.

Educational level was categorized as $\leq$9 years (partial or complete compulsory schooling), 10–12 years (partial or complete secondary schooling) and $>$12 years (attendance at college and/or university).

Geographic region of residence was used to be able to adjust for possible regional differences in hospital admissions. The region of residence was categorized as (1) large cities, defined as municipalities with a population of $>$200,000 and included Stockholm, Gothenburg and Malmö, i.e. the three largest cities in Sweden; (2) southern Sweden; and (3) northern Sweden.

Neighborhood deprivation

Data on neighborhood socio-economic status (NSES) was derived from Small Area Market Statistics (SAMS). The NSES index was categorized into three groups: more than one standard deviation (SD) below the mean (high NSES or low-deprivation level), more than one SD above the mean (low NSES or high-deprivation level), and within one SD of the mean (middle NSES or middle-deprivation level), with neighborhood status classified as high, middle or low NSES (corresponding to the categories low, middle and high-deprivation in the index).

Statistical analysis

The number of urolithiasis cases was presented for first-generation and second-generation immigrants and across baseline subject characteristics. We also categorized urolithiasis into upper urolithiasis, lower urolithiasis and urolithiasis due to other diseases. However, we decided to analyse using all incident urolithiasis cases as outcomes, as most stones belonged to the upper urolithiasis group. Cox regression analysis was used to estimate the risk (hazard ratios (HR) with 95% confidence intervals (CI)) of incident urolithiasis in different immigrant groups compared to the Swedish-born population during the follow-up time. All analyses were stratified by sex. Three models were used in our analyses:

Model 1 was adjusted for age and region of residence in Sweden.

Model 2 was adjusted for age, region of residence in Sweden, educational level, marital status and neighborhood

SES, to examine to what extent SES explained the association between country of birth and urolithiasis incidence.

Model 3 was constructed as Model 2 with the inclusion of relevant co-morbidities to examine if other diagnoses explained the association between country of birth and urolithiasis incidence.

The study was approved by the regional ethics boards at Karolinska Institutet and Lund University.

Table 1. Baseline characteristics and incident cases of urolithiasis in the study population.

	First generation individuals				Second generation individuals			
	Population		Events		Population		Events	
	No.	%	No	%	No.	%	No	%
Total population	6452996		101302		8399203		84216	
Upper urolithiasis			87695	86.6			67374	80.0
Lower urolithiasis			13456	13.3			5759	6.8
Other disease with urolithiasis			151	0.1			11083	13.3
Gender								
Males	3053439	47.3	71173	70.3	4292637	51.1	58830	69.9
Females	3399557	52.7	30129	29.7	4106566	48.9	25386	30.1
Immigrant status*		0.0						
Swedish	5309659	82.3	87003	85.9	6708819	79.9	75520	89.7
Foreign born	1143337	17.7	14299	14.1	1690384	20.1	6696	8.0
Educational level								
≤9	2018070	31.3	36302	35.8	3296804	39.3	25450	30.2
10–12	1629336	25.2	29081	28.7	1477060	17.6	27098	32.2
>12	2805590	43.5	35919	35.5	3625339	43.2	31668	37.6
Region of residence								
Large cities	2069959	32.1	34204	33.8	2046849	24.4	28885	34.3
Southern Sweden	2697908	41.8	45809	45.2	2653571	31.6	39647	47.1
Northern Sweden	1685129	26.1	21289	21.0	3698783	44.0	15684	18.6
Marital status								
Married	4760887	73.8	79652	78.6	6243961	74.3	60068	71.3
Not married	1692109	26.2	21650	21.4	2155242	25.7	24148	28.7
Neighborhood deprivation								
Low	891508	13.8	15554	15.4	939394	11.2	13847	16.4
Middle	3045109	47.2	51762	51.1	2978090	35.5	45156	53.6
High	722534	11.2	11475	11.3	684206	8.1	9415	11.2
Unknown	1793845	27.8	22511	22.2	3797513	45.2	15798	18.8
Hospital diagnosis of COPD								
No	6163920	95.5	94448	93.2	7978729	95.0	79191	94.0
Yes	289076	4.5	6854	6.8	420474	5.0	5025	6.0
Hospital diagnosis of obesity								
No	6367591	98.7	99366	98.1	8282999	98.6	82139	97.5
Yes	85405	1.3	1936	1.9	116204	1.4	2077	2.5
Hospital diagnosis of CHD								
No	5918432	91.7	84261	83.2	8180756	97.4	71883	85.4
Yes	534564	8.3	17041	16.8	218447	2.6	12333	14.6
Hospital diagnosis of diabetes								
No	6102823	94.6	89380	88.2	8176388	97.3	72161	85.7
Yes	350173	5.4	11922	11.8	222815	2.7	12055	14.3
Hospital diagnosis of alcohol-related diseases								
No	6316607	97.9	99512	98.2	8213844	97.8	82033	97.4
Yes	136389	2.1	1790	1.8	185359	2.2	2183	2.6
Hospital diagnosis of stroke								
No	6080958	94.2	91143	90.0	8265492	98.4	77930	92.5
Yes	372038	5.8	10159	10.0	133711	1.6	6286	7.5
Hospital diagnosis of hypertension								
No	5692192	88.2	75121	74.2	7945999	94.6	60893	72.3
Yes	760804	11.8	26181	25.8	453204	5.4	23323	27.7
Hospital diagnosis of heart failure								
No	6128396	95.0	94192	93.0	8321619	99.1	79383	94.3
Yes	324600	5.0	7110	7.0	77584	0.9	4833	5.7
Hospital diagnosis of atrial fibrillation								
No	6085599	94.3	91034	89.9	8260858	98.4	77717	92.3
Yes	367397	5.7	10268	10.1	138345	1.6	6499	7.7
Hospital diagnosis of gout								
No	6419641	99.5	100102	98.8	8380760	99.8	82760	98.3
Yes	33355	0.5	1200	1.2	18443	0.2	1456	1.7
Hospital diagnosis of hyperlipidemia								
No	6335796	98.2	96923	95.7	8384066	99.8	72832	86.5
Yes	117200	1.8	4379	4.3	15137	0.2	11384	13.5
Hospital diagnosis of ESRD								
No	6432973	99.7	100659	99.4	8308752	98.9	80166	95.2
Yes	20023	0.3	643	0.6	90451	1.1	4050	4.8
All	6452996	100.0	101302	100.0	8399203	100.0	84216	100.0

*Immigrant status in the second-generation individuals based on the country of birth of parents.

Results

Baseline characteristics of the first- and second- generation samples are shown in Table 1. The study of the first-generation sample comprised of 6,452,996 individuals aged 45 years and older, out of whom 1,143,337 (17.7%) were immigrants. The study of second-generation sample comprised of 8,399,203 individuals, out of whom 1,690,384 (20.1%) were second-generation immigrants. The proportion of incident cases of urolithiasis was larger in first- (1.6%) compared to second-generation immigrants (0.9%). Males were overrepresented among both samples, and immigrants were underrepresented in both samples. The distribution of subgroups of stones were different in the two samples, with highest frequency, however, for upper stones (86.6% in the first- and 80.0% in the second-generation sample), but with a much larger frequency of urolithiasis in other diseases in the second-generation sample (13.3% vs 0.1% in the first-generation sample).

The HRs for being diagnosed with urolithiasis among first-generation immigrant men and women are shown in Tables 2a and 2b, respectively. Compared to Swedish-born individuals, the risk for urolithiasis was lower among men and women from the Nordic countries, most Western European countries and North America; but higher in men and women from Central and Eastern Europe, Russia, Latin America, Africa and Asia.

The HRs for being diagnosed with urolithiasis among second-generation immigrant men and women are shown in Tables 3a and 3b, respectively. Compared to individuals with Swedish-born parents, the risk for urolithiasis was lower in men and women with parents from Latin America, Africa and Asia; but higher in men and women with parents from Denmark,

Table 2a. HR of Urolithiasis in first-generation male immigrants.

	Model 1			Model 2			Model 3		
	HR	95% CI		HR	95% CI		HR	95% CI	
Sweden	1			1			1		
All male immigrants	**1.02**	**1.00**	**1.04**	**1.07**	**1.05**	**1.10**	**1.06**	**1.04**	**1.09**
Nordic countries	**0.54**	**0.52**	**0.57**	**0.55**	**0.53**	**0.57**	**0.56**	**0.53**	**0.58**
Denmark	**0.80**	**0.74**	**0.87**	**0.80**	**0.74**	**0.87**	**0.82**	**0.76**	**0.89**
Finland	**0.48**	**0.46**	**0.51**	**0.49**	**0.47**	**0.52**	**0.49**	**0.47**	**0.52**
Iceland	**0.28**	**0.19**	**0.41**	**0.28**	**0.19**	**0.42**	**0.30**	**0.20**	**0.44**
Norway	**0.58**	**0.53**	**0.65**	**0.60**	**0.54**	**0.66**	**0.61**	**0.55**	**0.68**
Southern Europe	1.01	0.94	1.08	1.03	0.96	1.11	1.06	0.99	1.14
France	1.00	0.81	1.24	1.04	0.84	1.29	1.06	0.86	1.32
Greece	0.98	0.87	1.10	1.00	0.89	1.12	1.04	0.93	1.17
Italy	0.90	0.78	1.04	0.94	0.81	1.09	0.95	0.82	1.11
Spain	**1.20**	**1.00**	**1.42**	**1.23**	**1.03**	**1.47**	**1.28**	**1.07**	**1.52**
Other Southern European countries	**1.23**	**1.00**	**1.52**	1.22	0.99	1.50	**1.24**	**1.01**	**1.54**
Western Europe	**0.87**	**0.82**	**0.93**	**0.88**	**0.83**	**0.94**	**0.89**	**0.84**	**0.95**
The Netherlands	0.87	0.69	1.08	0.89	0.71	1.11	0.91	0.73	1.13
UK and Ireland	**0.65**	**0.56**	**0.75**	**0.66**	**0.57**	**0.76**	**0.68**	**0.59**	**0.79**
Germany	0.97	0.89	1.06	0.99	0.90	1.07	0.99	0.91	1.07
Austria	1.08	0.91	1.28	1.11	0.93	1.32	1.11	0.93	1.31
Other Western European countries	0.72	0.53	0.97	0.75	0.56	1.01	0.77	0.57	1.04
Eastern Europe	**1.97**	**1.90**	**2.05**	**1.90**	**1.83**	**1.97**	**1.85**	**1.78**	**1.92**
Bosnia	**2.23**	**2.09**	**2.39**	**2.19**	**2.05**	**2.34**	**2.11**	**1.97**	**2.25**
Former Yugoslavia	**1.76**	**1.68**	**1.85**	**1.71**	**1.63**	**1.80**	**1.68**	**1.59**	**1.76**
Croatia	**1.54**	**1.26**	**1.88**	**1.45**	**1.19**	**1.77**	**1.44**	**1.18**	**1.76**
Romania	**2.10**	**1.85**	**2.39**	**2.06**	**1.81**	**2.35**	**2.02**	**1.78**	**2.30**
Bulgaria	**1.92**	**1.52**	**2.43**	**1.90**	**1.51**	**2.41**	**1.91**	**1.51**	**2.41**
Other Eastern European countries	**3.86**	**3.41**	**4.37**	**3.57**	**3.15**	**4.04**	**3.46**	**3.06**	**3.92**
Baltic countries	0.89	0.75	1.04	0.91	0.77	1.07	0.90	0.76	1.06
Estonia	**0.75**	**0.62**	**0.92**	**0.78**	**0.64**	**0.95**	**0.77**	**0.63**	**0.94**
Latvia	**1.38**	**1.03**	**1.84**	**1.41**	**1.06**	**1.88**	**1.39**	**1.04**	**1.85**
Central Europe	**1.47**	**1.38**	**1.57**	**1.46**	**1.37**	**1.55**	**1.43**	**1.34**	**1.53**
Poland	**1.69**	**1.56**	**1.84**	**1.67**	**1.54**	**1.82**	**1.65**	**1.52**	**1.80**
Other Central European countries	1.08	0.89	1.30	1.10	0.91	1.33	1.09	0.91	1.32
Hungary	**1.30**	**1.16**	**1.47**	**1.30**	**1.15**	**1.47**	**1.27**	**1.13**	**1.43**
Africa	**1.39**	**1.30**	**1.49**	**1.40**	**1.30**	**1.50**	**1.37**	**1.28**	**1.47**
Northern America	**0.67**	**0.57**	**0.78**	**0.69**	**0.59**	**0.80**	**0.71**	**0.61**	**0.83**
Latin America	**1.65**	**1.54**	**1.76**	**1.67**	**1.56**	**1.79**	**1.69**	**1.58**	**1.81**
Chile	**1.99**	**1.84**	**2.16**	**2.02**	**1.86**	**2.19**	**2.03**	**1.87**	**2.20**
South America	**1.16**	**1.02**	**1.31**	**1.19**	**1.05**	**1.35**	**1.21**	**1.07**	**1.38**
Asia	**2.58**	**2.52**	**2.65**	**2.54**	**2.47**	**2.61**	**2.48**	**2.41**	**2.55**
Turkey	**2.29**	**2.15**	**2.44**	**2.23**	**2.09**	**2.38**	**2.18**	**2.05**	**2.33**
Lebanon	**2.92**	**2.71**	**3.15**	**2.86**	**2.65**	**3.09**	**2.76**	**2.56**	**2.98**
Iran	**2.46**	**2.32**	**2.59**	**2.48**	**2.34**	**2.62**	**2.47**	**2.33**	**2.61**
Iraq	**4.14**	**3.97**	**4.32**	**4.12**	**3.94**	**4.30**	**3.93**	**3.76**	**4.11**
Other Asian countries	**1.61**	**1.52**	**1.70**	**1.60**	**1.51**	**1.70**	**1.57**	**1.48**	**1.66**
Russia	**1.47**	**1.26**	**1.73**	**1.50**	**1.28**	**1.77**	**1.48**	**1.26**	**1.74**

Model 1: adjusted for age and region of residence in Sweden; Model 2: adjusted for age, region of residence in Sweden, educational level, and marital status, and neighborhood deprivation; Model 3: model 2 + comorbidities.
Bold values are statistically significant.

Table 2b. HR of Urolithiasis in first-generation female immigrants.

	Model 1			Model 2			Model 3		
	HR	95% CI		HR	95% CI		HR	95% CI	
Sweden	1			1			1		
All female immigrants	**1.07**	**1.03**	**1.10**	**1.14**	**1.10**	**1.18**	**1.12**	**1.08**	**1.16**
Nordic countries	**0.63**	**0.60**	**0.66**	**0.61**	**0.58**	**0.64**	**0.61**	**0.58**	**0.64**
Denmark	**0.84**	**0.74**	**0.95**	**0.82**	**0.73**	**0.93**	**0.85**	**0.75**	**0.96**
Finland	**0.60**	**0.56**	**0.63**	**0.58**	**0.54**	**0.62**	**0.57**	**0.54**	**0.61**
Iceland	**0.38**	**0.24**	**0.61**	**0.38**	**0.24**	**0.60**	**0.41**	**0.26**	**0.65**
Norway	**0.65**	**0.57**	**0.74**	**0.64**	**0.56**	**0.72**	**0.65**	**0.57**	**0.74**
Southern Europe	0.93	0.81	1.07	0.91	0.79	1.05	0.98	0.85	1.12
France	0.73	0.48	1.11	0.77	0.51	1.17	0.81	0.54	1.23
Greece	0.95	0.77	1.18	0.92	0.74	1.13	1.00	0.81	1.24
Italy	0.83	0.58	1.17	0.83	0.58	1.17	0.89	0.63	1.26
Spain	1.28	0.93	1.75	1.28	0.94	1.75	1.35	0.98	1.84
Other Southern European countries	0.84	0.55	1.29	0.82	0.54	1.26	0.85	0.55	1.30
Western Europe	0.95	0.86	1.05	0.97	0.88	1.07	0.99	0.90	1.09
The Netherlands	0.82	0.55	1.23	0.85	0.57	1.27	0.89	0.60	1.33
UK and Ireland	**0.56**	**0.42**	**0.75**	**0.58**	**0.43**	**0.77**	**0.62**	**0.46**	**0.83**
Germany	1.10	0.98	1.24	1.12	1.00	1.26	1.12	1.00	1.26
Austria	1.24	0.92	1.68	1.26	0.93	1.70	1.27	0.94	1.72
Other Western European countries	**0.42**	**0.22**	**0.81**	**0.44**	**0.23**	**0.84**	**0.46**	**0.24**	**0.89**
Eastern Europe	**2.29**	**2.18**	**2.40**	**2.26**	**2.15**	**2.37**	**2.22**	**2.12**	**2.34**
Bosnia	**2.29**	**2.10**	**2.49**	**2.36**	**2.16**	**2.57**	**2.31**	**2.12**	**2.53**
Former Yugoslavia	**2.27**	**2.12**	**2.42**	**2.19**	**2.05**	**2.34**	**2.16**	**2.02**	**2.31**
Croatia	**1.41**	**1.04**	**1.91**	**1.41**	**1.04**	**1.91**	**1.42**	**1.05**	**1.93**
Romania	**2.13**	**1.80**	**2.52**	**2.23**	**1.89**	**2.64**	**2.20**	**1.86**	**2.60**
Bulgaria	**2.47**	**1.87**	**3.26**	**2.57**	**1.94**	**3.39**	**2.60**	**1.97**	**3.43**
Other Eastern European countries	**3.73**	**3.16**	**4.40**	**3.55**	**3.00**	**4.20**	**3.50**	**2.96**	**4.14**
Baltic countries	**0.76**	**0.59**	**0.97**	0.80	0.63	1.03	0.78	0.61	1.00
Estonia	**0.63**	**0.46**	**0.87**	**0.66**	**0.48**	**0.92**	**0.65**	**0.47**	**0.90**
Latvia	1.08	0.74	1.59	1.17	0.80	1.72	1.15	0.78	1.69
Central Europe	**1.51**	**1.39**	**1.64**	**1.55**	**1.43**	**1.68**	**1.54**	**1.42**	**1.68**
Poland	**1.63**	**1.49**	**1.79**	**1.68**	**1.53**	**1.84**	**1.68**	**1.53**	**1.84**
Other Central European	1.06	0.80	1.41	1.11	0.84	1.48	1.13	0.85	1.50
Hungary	**1.34**	**1.10**	**1.63**	**1.38**	**1.13**	**1.68**	**1.34**	**1.10**	**1.63**
Africa	**1.43**	**1.29**	**1.59**	**1.39**	**1.25**	**1.54**	**1.37**	**1.23**	**1.52**
Northern America	**0.63**	**0.49**	**0.81**	**0.66**	**0.52**	**0.85**	**0.70**	**0.54**	**0.90**
Latin America	**2.00**	**1.84**	**2.17**	**1.97**	**1.81**	**2.14**	**1.94**	**1.78**	**2.11**
Chile	**2.41**	**2.18**	**2.67**	**2.35**	**2.12**	**2.60**	**2.26**	**2.04**	**2.50**
South America	**1.47**	**1.27**	**1.71**	**1.50**	**1.30**	**1.74**	**1.52**	**1.31**	**1.76**
Asia	**2.07**	**1.99**	**2.15**	**2.03**	**1.95**	**2.11**	**1.99**	**1.91**	**2.08**
Turkey	**2.41**	**2.20**	**2.64**	**2.23**	**2.03**	**2.44**	**2.17**	**1.98**	**2.38**
Lebanon	**2.43**	**2.16**	**2.73**	**2.30**	**2.05**	**2.60**	**2.25**	**2.00**	**2.53**
Iran	**2.24**	**2.06**	**2.44**	**2.34**	**2.15**	**2.55**	**2.32**	**2.13**	**2.52**
Iraq	**3.28**	**3.07**	**3.51**	**3.28**	**3.06**	**3.52**	**3.14**	**2.93**	**3.36**
Other Asian countries	**1.28**	**1.19**	**1.37**	**1.26**	**1.18**	**1.36**	**1.26**	**1.17**	**1.36**
Russia	**1.25**	**1.04**	**1.49**	**1.34**	**1.12**	**1.61**	**1.33**	**1.11**	**1.59**

Model 1: adjusted for age and region of residence in Sweden; Model 2: adjusted for age, region of residence in Sweden, educational level, and marital status; Model 3: model 2 + neighborhood deprivation.
Bold values are statistically significant.

Germany and Hungary, in men with parents from Austria, and in women with parents from the Netherlands and Poland.

The differences in risk for urolithiasis between first- and second-generation immigrants while focusing on specific population groups were also reported. For example, looking at Asia, risk was higher in first-generation immigrants compared to Swedish-born, while it was the other way around for second-generation immigrants.

As regards types of urolithiasis, upper stones were most frequent, but with other diseases as causes more frequent in the second-generation study (10.6–15.8%) compared to the first-generation (0.1–0.2%) (Supplementary Tables S1a 'Population in first-generation and number of cases of urolithiasis events categorized by sex', 1b 'Population in second-generation and number of cases of urolithiasis events categorized by sex', 2a 'Population in first-generation and number of cases of urolithiasis events in men', 2b 'Population in first-generation and number of cases of urolithiasis events in women', 2c 'Population in second-generation and number of cases of urolithiasis events categorized in men' and 2d 'Population in second-generation and number of cases of urolithiasis events categorized in women'). In the first-generation study, lower stones were more common in Swedish-born men compared to foreign-born, i.e. 18.2% vs 9.6% (Supplementary Table S2a 'Population in first-generation and number of cases of urolithiasis events in men'). Regarding co-morbidities, rates among individuals with urolithiasis were higher for most diseases, especially for cardiovascular diseases, with highest rates for hypertension and CHD, but also for diabetes. There were no seemingly different patterns of co-morbidities between Swedish-born or foreign-born men and women.

Table 3a. HR of Urolithiasis in second-generation male immigrants.

	Model 1			Model 2			Model 3		
	HR	95% CI		HR	95% CI		HR	95% CI	
Sweden	1			1			1		
All male immigrants	**0.93**	**0.90**	**0.96**	**0.95**	**0.92**	**0.98**	**0.95**	**0.92**	**0.98**
Nordic countries	**0.93**	**0.89**	**0.96**	**0.94**	**0.90**	**0.97**	**0.94**	**0.90**	**0.98**
Denmark	**1.24**	**1.15**	**1.35**	**1.24**	**1.14**	**1.34**	**1.23**	**1.13**	**1.33**
Finland	**0.77**	**0.73**	**0.82**	**0.78**	**0.74**	**0.83**	**0.80**	**0.76**	**0.85**
Iceland	**0.14**	**0.04**	**0.55**	**0.15**	**0.04**	**0.61**	**0.16**	**0.04**	**0.64**
Norway	1.07	0.99	1.15	1.08	1.00	1.16	1.06	0.98	1.14
Southern Europe	1.02	0.88	1.19	1.08	0.93	1.26	1.09	0.94	1.27
France	1.11	0.78	1.58	1.18	0.83	1.68	1.31	0.92	1.86
Greece	0.84	0.62	1.14	0.90	0.66	1.22	0.93	0.69	1.26
Italy	1.19	0.94	1.50	1.25	0.98	1.58	1.19	0.94	1.50
Spain	1.00	0.66	1.52	1.06	0.69	1.60	1.11	0.73	1.68
Other Southern European countries	0.65	0.29	1.44	0.67	0.30	1.48	0.63	0.29	1.41
Western Europe	1.07	0.99	1.16	**1.10**	**1.02**	**1.19**	**1.12**	**1.04**	**1.21**
The Netherlands	0.97	0.69	1.38	1.00	0.71	1.42	1.00	0.71	1.42
UK and Ireland	**0.57**	**0.41**	**0.79**	**0.61**	**0.44**	**0.85**	**0.61**	**0.44**	**0.84**
Germany	**1.13**	**1.03**	**1.24**	**1.15**	**1.05**	**1.26**	**1.19**	**1.08**	**1.30**
Austria	**1.33**	**1.07**	**1.64**	**1.36**	**1.10**	**1.68**	**1.25**	**1.01**	**1.54**
Other Western European countries	0.85	0.54	1.34	0.90	0.57	1.41	0.99	0.63	1.55
Eastern Europe	0.86	0.73	1.00	0.89	0.76	1.03	0.85	0.73	1.00
Bosnia	**0.58**	**0.35**	**0.97**	0.69	0.41	1.14	0.64	0.39	1.06
Former Yugoslavia	0.86	0.72	1.04	0.87	0.72	1.05	0.84	0.69	1.00
Croatia	1.04	0.47	2.31	1.02	0.46	2.28	0.99	0.45	2.21
Romania	1.01	0.64	1.61	1.06	0.67	1.68	1.06	0.67	1.68
Bulgaria	1.14	0.48	2.75	1.23	0.51	2.95	1.30	0.54	3.12
Other Eastern European countries	1.04	0.34	3.23	1.06	0.34	3.29	0.95	0.31	2.96
Baltic countries	0.89	0.78	1.02	0.92	0.81	1.05	0.97	0.85	1.10
Estonia	**0.83**	**0.72**	**0.96**	**0.86**	**0.74**	**0.99**	0.92	0.79	1.06
Latvia	1.25	0.94	1.67	1.30	0.98	1.74	1.24	0.93	1.65
Central Europe	**1.39**	**1.24**	**1.56**	**1.41**	**1.26**	**1.58**	**1.40**	**1.24**	**1.57**
Poland	**1.48**	**1.26**	**1.74**	**1.51**	**1.29**	**1.78**	**1.45**	**1.23**	**1.70**
Other Central European countries	1.18	0.90	1.54	1.20	0.92	1.57	1.25	0.95	1.63
Hungary	**1.40**	**1.14**	**1.71**	**1.39**	**1.14**	**1.71**	**1.40**	**1.14**	**1.72**
Africa	**0.40**	**0.24**	**0.65**	**0.44**	**0.27**	**0.71**	**0.43**	**0.26**	**0.71**
Northern America	0.90	0.78	1.03	0.92	0.80	1.05	0.92	0.80	1.05
Latin America	**0.65**	**0.46**	**0.91**	**0.69**	**0.49**	**0.96**	**0.69**	**0.49**	**0.96**
Chile	0.71	0.46	1.09	0.75	0.49	1.15	0.76	0.49	1.16
South America	0.56	0.32	0.96	0.60	0.35	1.03	0.59	0.34	1.02
Asia	**0.54**	**0.44**	**0.65**	**0.58**	**0.48**	**0.70**	**0.56**	**0.46**	**0.68**
Turkey	0.80	0.60	1.05	0.84	0.64	1.11	0.82	0.62	1.08
Lebanon	**0.30**	**0.12**	**0.71**	**0.32**	**0.14**	**0.78**	**0.30**	**0.13**	**0.72**
Iran	**0.27**	**0.13**	**0.54**	**0.29**	**0.15**	**0.58**	**0.28**	**0.14**	**0.56**
Iraq	**0.24**	**0.11**	**0.53**	**0.28**	**0.13**	**0.61**	**0.25**	**0.11**	**0.56**
Other Asia countries	**0.57**	**0.42**	**0.77**	**0.62**	**0.46**	**0.84**	**0.60**	**0.44**	**0.81**
Russia	0.89	0.71	1.11	0.90	0.72	1.14	0.94	0.75	1.18

Model 1: adjusted for age and region of residence in Sweden; Model 2: adjusted for age, region of residence in Sweden, educational level, and marital status, and neighborhood deprivation; Model 3: model 2 + comorbidities.
Bold values are statistically significant.

Discussion

In this national study with more than 6 million individuals in the first-generation study, we found urolithiasis to be more common in many immigrant groups in Sweden, including immigrants from Central and Eastern Europe, Latin America, Africa and Asia. However, the risk was lower among first-generation immigrants from the Nordic countries, some Western European countries and North America. Second-generation immigrants from Asia and Latin America showed lower risk, in contrast to the higher risk among first-generation immigrants from these regions of the world.

There are few studies on urolithiasis among immigrants in the Western world. In the mentioned British study, some groups, i.e. immigrants from Bulgaria, Romania, Turkey, Pakistan and India, i.e. from countries with a high incidence, showed an increased risk, a study from New Zealand found individuals of Middle Eastern descent to show the highest incidence, while individuals from other Asian countries and individuals of European descent showed a similar risk [10]. We found patterns similar to this, with a high incidence in the mentioned groups, but also with a higher incidence in many other groups, in other Central and Eastern European countries, and in immigrants from Africa and Latin America. Among the second-generation immigrants excess risk could also, to some extent, be found in immigrants with parents from Central and Eastern European but also from some Western European countries, but, however, lower risks among second-generation immigrants from Asia, Africa and Latin America.

Urolithiasis is associated with different diseases, especially cardio-metabolic diseases such as obesity, diabetes, gout, hypertension, chronic kidney disease (CKD) with end-stage renal disease (ESRD), and also other cardiovascular

Table 3b. HR of Urolithiasis in second-generation female immigrants.

	Model 1			Model 2			Model 3		
	HR	95% CI		HR	95% CI		HR	95% CI	
Sweden	1			1			1		
All female immigrants	0.98	0.93	1.03	1.01	0.96	1.06	1.01	0.96	1.06
Nordic countries	1.02	0.96	1.08	1.03	0.97	1.09	1.03	0.97	1.09
Denmark	**1.28**	**1.13**	**1.44**	**1.26**	**1.12**	**1.42**	**1.31**	**1.16**	**1.48**
Finland	0.92	0.85	0.99	0.94	0.87	1.01	0.93	0.86	1.01
Iceland	0.15	0.02	1.03	0.16	0.02	1.13	0.17	0.02	1.23
Norway	1.09	0.97	1.22	1.09	0.97	1.22	1.07	0.96	1.20
Southern Europe	0.87	0.68	1.11	0.93	0.73	1.19	0.95	0.74	1.21
France	0.82	0.44	1.52	0.90	0.48	1.67	0.96	0.52	1.78
Greece	0.70	0.43	1.15	0.76	0.46	1.23	0.81	0.49	1.32
Italy	1.06	0.72	1.56	1.13	0.77	1.66	1.12	0.76	1.64
Spain	0.83	0.41	1.66	0.88	0.44	1.76	0.81	0.41	1.63
Other Southern European countries	0.85	0.32	2.26	0.85	0.32	2.27	0.93	0.35	2.47
Western Europe	**1.15**	**1.03**	**1.29**	**1.20**	**1.07**	**1.35**	**1.20**	**1.07**	**1.34**
The Netherlands	**1.56**	**1.03**	**2.37**	**1.64**	**1.08**	**2.48**	**1.41**	**0.93**	**2.14**
UK and Ireland	0.78	0.51	1.18	0.84	0.55	1.28	0.93	0.61	1.41
Germany	**1.22**	**1.07**	**1.39**	**1.26**	**1.10**	**1.44**	**1.24**	**1.08**	**1.41**
Austria	0.88	0.59	1.30	0.92	0.62	1.36	1.01	0.68	1.49
Other Western European countries	1.24	0.70	2.19	1.35	0.76	2.37	1.34	0.76	2.36
Eastern Europe	0.90	0.72	1.13	0.93	0.74	1.16	0.93	0.74	1.16
Bosnia	0.51	0.23	1.14	0.61	0.27	1.35	0.57	0.26	1.27
Former Yugoslavia	0.96	0.74	1.24	0.96	0.74	1.24	0.96	0.74	1.25
Croatia	1.72	0.72	4.13	1.68	0.70	4.03	1.81	0.75	4.34
Romania	0.89	0.42	1.86	0.94	0.45	1.97	0.91	0.43	1.91
Bulgaria	0.89	0.22	3.57	0.97	0.24	3.90	1.08	0.27	4.30
Other Eastern European countries									
Baltic countries	**0.66**	**0.52**	**0.83**	**0.70**	**0.55**	**0.88**	**0.72**	**0.57**	**0.91**
Estonia	**0.69**	**0.54**	**0.88**	**0.73**	**0.57**	**0.93**	**0.75**	**0.59**	**0.96**
Latvia	0.49	0.24	0.97	0.52	0.26	1.04	0.54	0.27	1.08
Central Europe	**1.31**	**1.10**	**1.56**	**1.33**	**1.11**	**1.58**	**1.32**	**1.11**	**1.58**
Poland	1.09	0.83	1.44	1.11	0.84	1.46	1.13	0.86	1.49
Other Central European countries	1.05	0.69	1.62	1.08	0.71	1.66	1.10	0.72	1.68
Hungary	**1.81**	**1.39**	**2.37**	**1.82**	**1.39**	**2.37**	**1.72**	**1.32**	**2.25**
Africa	**0.30**	**0.14**	**0.67**	**0.33**	**0.15**	**0.73**	**0.33**	**0.15**	**0.72**
Northern America	**0.79**	**0.64**	**0.99**	0.82	0.65	1.02	0.88	0.71	1.10
Lartin America	**0.40**	**0.22**	**0.75**	**0.42**	**0.22**	**0.78**	**0.43**	**0.23**	**0.80**
Chile	0.55	0.28	1.10	0.56	0.28	1.13	0.56	0.28	1.12
South America	**0.19**	**0.05**	**0.76**	**0.20**	**0.05**	**0.81**	**0.22**	**0.06**	**0.88**
Asia	**0.39**	**0.28**	**0.54**	**0.41**	**0.30**	**0.57**	**0.41**	**0.29**	**0.56**
Turkey	0.72	0.47	1.10	0.74	0.48	1.13	0.74	0.48	1.14
Lebanon	**0.12**	**0.02**	**0.84**	**0.12**	**0.02**	**0.88**	**0.12**	**0.02**	**0.88**
Iran	**0.22**	**0.07**	**0.67**	**0.23**	**0.07**	**0.71**	**0.21**	**0.07**	**0.66**
Iraq	**0.08**	**0.01**	**0.56**	**0.09**	**0.01**	**0.64**	**0.09**	**0.01**	**0.61**
Other Asian countries	**0.35**	**0.20**	**0.62**	**0.38**	**0.21**	**0.66**	**0.37**	**0.21**	**0.66**
Russia	1.13	0.83	1.53	1.17	0.86	1.58	1.13	0.84	1.54

Model 1: adjusted for age and region of residence in Sweden; Model 2: adjusted for age, region of residence in Sweden, educational level, and marital status; Model 3: model 2 + neighborhood deprivation.
Bold values are statistically significant.

diseases and risk factors, including smoking and dyslipidaemia [6]. Besides, patterns of co-morbidities did not differ obviously between Swedish-born and foreign-born individuals.

The conflicting results for the first- and second-generation immigrant groups could indicate that environmental factors rather than genetic factors are most important for stone formation. Different factors may be involved, such as environmental factors with urbanisation in first-generation immigrants moving from a lower to a higher industrialised country [12], and also dietary changes with adaptation to Western dietary habits [7], which then would rather affect the second-generation immigrants. A high intake of meat is associated with a lower risk of urolithiasis, compared to those with lower meat intake, or a high intake of fish or vegetables [13]. However, possible association with different dietary habits are difficult to understand considering the increased risk in many different groups, with seemingly no common dietary patterns. Thus, we have no good explanation for the seemingly contradictory results between the first- and second-generation immigrants to what could be expected.

There are also genetic factors with familial clustering of urolithiasis [14]. Nephrolithiasis has been more common in developed countries, but the prevalence of urolithiasis in at least some developing countries, especially in tropical regions, has been found to be similar to rates of Western countries, with an association with the warmest part of the year [6].

We found cardiovascular diseases, diabetes and hyperlipidemia to be more associated with urolithiasis (Table 1), in accordance with a review, reporting that urolithiasis is related to diseases such as the metabolic syndrome, cardiovascular disease, and chronic kidney disease [15].

Nephrolithiasis has been found to be related to incident hypertension, while the reverse causation does not seem to be true [15].

We chose to include all types of urolithiasis, although upper stones, nephrolithiasis, dominated especially among first-generation immigrants. In the second-generation study, i.e. of second-generation immigrants and Swedish-born individuals with Swedish-born parents, a higher rate of urolithiasis owing to other diseases was found, most probably an effect of the lower age in these groups.

There are some limitations in this study. We used data from the National Patient register, where data from primary care are not included, meaning that the rates of diabetes and hypertension are underestimated [16]. Besides, the rate of obesity is low, as this diagnosis is rarely set in the patient records.

There are also several strengths with the study. We used national Swedish data, with the high quality of Swedish registers [17,18]. All types of urolithiasis were included, although nephrolithiasis dominated, in order not to miss important findings. Many diseases are noted in the National Patient register with data from hospitals, including diagnosis from out-patient clinics. Thus diagnoses of urolithiasis could be expected to show a high coverage, as well as data for ESRD. We also included co-morbidities of known importance.

For clinical practice it is of importance to know that the risk for urolithiasis is increased in many first-generation immigrant groups. Furthermore, it is of importance to perform further studies to be able to understand the mechanisms behind the results found.

In conclusion, we found presence of urolithiasis to be more common among many groups of first-generation men and women in Sweden compared to Swedish-born, while most second-generation men showed a lower rate compared to Swedish-born men with Swedish-born parents. This has to be further studied, and in clinical practice attention should also be paid to this.

Disclosure statement

No potential conflict of interest was reported by the authors.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent was not applicable, as the study was based on anonymised data from registers.

The study was approved by the regional ethics boards at Karolinska Institutet and Lund University.

Funding

This work was supported by ALF funding awarded to Jan Sundquist and Kristina Sundquist and by grants from the Swedish Research Council (awarded to Kristina Sundquist), the Swedish Council for Working Life and Social Research (Jan Sundquist).

References

[1] Morgan MS, Pearle MS. Medical management of renal stones. BMJ. 2016;352:i52.
[2] Tiselius HG. Epidemiology and medical management of stone disease. BJU Int. 2003;91:758–767.
[3] Lopez M, Hoppe B. History, epidemiology and regional diversities of urolithiasis. Pediatr Nephrol. 2010;25:49–59.
[4] Raheem OA, Khandwala YS, Sur RL, et al. Burden of urolithiasis: trends in prevalence, treatments, and costs. Eur Urol Focus. 2017;3:18–26.
[5] Romero V, Akpinar H, Assimos DG. Kidney stones: a global picture of prevalence, incidence, and associated risk factors. Rev Urol. 2010;12:e86–e96.
[6] Trinchieri A. Epidemiology of urolithiasis: an update. Clin Cases Miner Bone Metab. 2008;5:101–106.
[7] Alatab S, Pourmand G, El Howairis Mel F, et al. National profiles of urinary calculi: a comparison between developing and developed worlds. Iran J Kidney Dis. 2016;10(2):51–61.
[8] Barraclough KA, Blashki GA, Holt SG, et al. Climate change and kidney disease-threats and opportunities. Kidney Int. 2017;92:526–530.
[9] Cook J, Lamb BW, Lettin JE, et al. The epidemiology of urolithiasis in an ethnically diverse population living in the same area. Urol J. 2016;13:2754–2758.
[10] Loeff S, Saluja M, Rice M. Review of acute symptomatic urolithiasis in Auckland. N Z Med J. 2018;131:44–50.
[11] Statistics Sweden. Foreign-Born Persons in Sweden by Country of Birth, Age and Sex. Year 2000 - 2015: Statistics Sweden. 2016.
[12] Goldfarb DS, Hirsch J. Hypothesis: urbanization and exposure to urban heat islands contribute to increasing prevalence of kidney stones. Med Hypotheses. 2015;85:953–957.
[13] Turney BW, Appleby PN, Reynard JM, et al. Diet and risk of kidney stones in the Oxford cohort of the European Prospective Investigation into Cancer and Nutrition (EPIC). Eur J Epidemiol. 2014;29:363–369.
[14] Hemminki K, Hemminki O, Forsti A, et al. Familial risks in urolithiasis in the population of Sweden. BJU Int. 2018;121:479–485.
[15] Shoag J, Tasian GE, Goldfarb DS, et al. The new epidemiology of nephrolithiasis. Adv Chronic Kidney Dis. 2015;22:273–278.
[16] Carlsson AC, Wandell P, Osby U, et al. High prevalence of diagnosis of diabetes, depression, anxiety, hypertension, asthma and COPD in the total population of Stockholm, Sweden - a challenge for public health. BMC Public Health. 2013;13:670.
[17] Ludvigsson JF, Almqvist C, Bonamy AK, et al. Registers of the Swedish total population and their use in medical research. Eur J Epidemiol. 2016;31:125–136.
[18] Ludvigsson JF, Andersson E, Ekbom A, et al. External review and validation of the Swedish national inpatient register. BMC Public Health. 2011;11:450.